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THE TREATMENT OF LUPUS ERYTHEMATOSUS WITH MEPACRINE AND PARA-AMINOBENZOIC ACID.

H. BLACK, M.B., M.R.A.C.P., M.R.C.P.Ed.

IN 1951 Page reported on 18 patients with lupus erythematosus treated with mepacrine, a drug not previously used in this disease. In the following article the results of 60 patients treated with mepacrine and 32 treated with para-aminobenzoic acid (PABA) at the General Infirmary at Leeds are recorded. Wherever possible the fourfold method of determining statistical significance has been applied to the results.

The patients have been divided into the following categories :

- (1) Those whose lupus erythematosus cleared completely.
- (2) Those who were considerably improved, which means complete clearance apart from relics or faint erythema.
- (3) Those who were moderately improved.
- (4) Those who showed a slight but definite improvement.
- (5) Those whose condition was unaltered by the treatment.
- (6) Those whose condition deteriorated during the course of the treatment.

From Table I it will be seen that 70% of the mepacrine and 43.8% of the PABA patients showed various degrees of improvement, and that 45% of

TABLE I.

	Mepacrine.			PABA.	
	No.	%.		No.	%.
Total cases	60	100	.	32	100
Completely cleared	10	16.7	.	3	9.4
Considerably improved	17	28.3	.	4	12.5
Moderately improved	6	10	.	4	12.5
Slightly improved	9	15	.	3	9.4
Unaltered	13	21.7	.	12	37.5
Worse	5	8.3	.	6	18.7

the mepacrine and 21.9% of the PABA patients were completely or almost completely cleared. Thirty per cent. of the mepacrine and 56.2% of the PABA patients failed to respond.

Categories 1 and 2 correspond with Page's classification of "excellent result," and category 3 with that of "good result." He reported in his series of 18 patients who had received 20 treatments 95% showing varying degrees of improvement, of whom 45% were completely cleared or considerably improved and 35% moderately improved. Only one case failed to respond.

From Table I it appears that mepacrine is definitely the better treatment, but statistical analysis ($\chi^2 = 2.786$; $P = 0.10 - 0.05$) shows that while the probability of this being so is suggestive it is not definitely significant.

In applying the fourfold test to decide whether a treatment is beneficial it is necessary to divide the patients into two groups, one of good results, and one of bad results. The line has to be drawn somewhere, and here it was decided that good results should comprise those in categories 1, 2 and 3, and bad results those in categories 4, 5 and 6, because it was considered that a worthwhile treatment should produce more than a slight improvement. If all those patients showing improvement whatever the degree are classed as good results, then P becomes statistically significant ($\chi^2 = 4.986$; $P = 0.05 - 0.02$). In all the other results the line has been drawn between those moderately and slightly improved.

Sex distribution.—The sex ratio of the mepacrine (1 : 2) and PABA (1 : 2.6) series is almost the same, since the two groups are unselected.

Mepacrine was more effective in females than in males. Analysis shows that it is highly unlikely that this is a chance occurrence ($\chi^2 = 6.136$; $P = 0.02 - 0.01$). This is not because of the presence or absence of scarring in the females ($\chi^2 = 2.344$; $P = 0.20 - 0.10$).

There are insufficient numbers for the test to be applied to the PABA patients, but the ratio of one good result to two bad ones is the same with both males and females, suggesting that PABA, unlike mepacrine, has no selective beneficial action in females.

Age distribution.—The numbers in each group are too small for tests of significance to be applied, so that it cannot be said that any one age group has responded better than any other to either treatment. The age distribution of the two groups was very similar.

Dosage in relation to cure.—*Mepacrine (Table II):* Comparison here is difficult, because of various amounts administered for various periods. Table II shows that some patients cleared completely, or were considerably improved, with doses as small as 100 mg. twice daily for one month, while others required as much as 100 mg. 3 times a day for 4 months. Some who received amounts as large as this failed to show any worthwhile degree of improvement. Although two patients might have been given the same total dose, the amounts

TABLE II.—*Mepacrine*.

	Duration of treatment (months).	Daily dosage (mg.).	Coloration of skin.	Duration prior to treatment (years).	Sex.
Completely cleared	1	100 × 3	Marked	$\frac{2}{1\frac{1}{2}}$	F.
	2	100 × 2	"	$\frac{5}{5}$	F.
	2	100 × 2	Moderate	$5\frac{1}{2}$	F.
	2	100 × 2	Slight	1	F.
	2	100 × 3	Marked	5	F., scarred
	$2\frac{1}{2}$	100	None	1	F.
	3	100 × 2	Marked	$\frac{7}{1\frac{1}{2}}$	F.
	3	$\left\{ \begin{array}{l} 100 \times 3, \text{ 2 months} \\ 100 \times 2, \text{ 1 month} \end{array} \right\}$	"	$\frac{4}{1\frac{1}{2}}$	F.
	3	100 × 3	Moderate	19	F., scarred
Considerably improved	4	100 × 2	"	2	F.
	1	100 × 2	Marked	$6\frac{1}{2}$	F.
	1	100 × 2	"	$\frac{4}{1\frac{1}{2}}$	F., scarred
	1	100 × 3	"	$1\frac{4}{1\frac{1}{2}}$	F.
	$1\frac{1}{2}$	100	"	1	F., scarred
	$1\frac{3}{4}$	100	Moderate	26	F.
	2	100	"	$3\frac{1}{2}$	F., scarred
	2	100	"	$\frac{4}{1\frac{1}{2}}$	M.
	2	$\left\{ \begin{array}{l} 100 \times 3, \text{ 1 month} \\ 100 \times 2, \text{ 1 month} \end{array} \right\}$	Not noted	$2\frac{5}{1\frac{1}{2}}$	M.
	2	100 × 3	Marked	18	F.
	2	100 × 3	"	16	F.
	3	$\left\{ \begin{array}{l} 100 \times 2, \text{ 1 month} \\ 100, \text{ 2 months} \end{array} \right\}$	"	7	M.
	3	100 × 2	"	17	F.
	3	100 × 2	Slight	$7\frac{1}{2}$	F.
	3	100 × 3	Marked	$8\frac{8}{1\frac{1}{2}}$	F.
	$3\frac{1}{2}$	100 × 2	"	4	M.
	4	100 × 3	Slight	5	F.
	4	100 × 3	Marked	3	F.
Moderately improved	1	100 × 3	"	6	F.
	2	$\left\{ \begin{array}{l} 100 \times 2, \text{ 1 month} \\ 100, \text{ 1 month} \end{array} \right\}$	"	12	M.
	3	$\left\{ \begin{array}{l} 100 \times 3, \text{ 2 months} \\ 100 \times 2, \text{ 1 month} \end{array} \right\}$	Moderate	$5\frac{8}{1\frac{1}{2}}$	F., scarred
	3	100 × 3	Marked	$\frac{6}{1\frac{1}{2}}$	F.
	4	$\left\{ \begin{array}{l} 100 \times 3, \text{ 3 months} \\ 100 \times 2, \text{ 1 month} \end{array} \right\}$	"	20	M., scarred
	6	$\left\{ \begin{array}{l} 100 \times 3, \text{ 6 weeks} \\ 100 \times 2, \text{ 20 weeks} \end{array} \right\}$	"	7	F.
Slightly improved	$1\frac{1}{2}$	100	Moderate	$\frac{6}{1\frac{1}{2}}$	M., scarred
	2	100 × 3	Marked	$\frac{9}{1\frac{1}{2}}$	M.
	2	100 × 2	"	5	M.
	3	100 × 2	Moderate	7	F., scarred
	3	100 × 2	Marked	16	M., "
	3	100 × 3	"	2	F.
	4	100 × 3	"	11	M.
	6	$\left\{ \begin{array}{l} 100 \times 2, \text{ 6 weeks} \\ 100, \text{ 6 months} \\ \text{alt. days,} \\ \text{3 months} \end{array} \right\}$	Moderate	30	F., scarred
	6	$\left\{ \begin{array}{l} 100 \times 2, \text{ 13 weeks} \\ 100, \text{ 11 weeks} \end{array} \right\}$	Marked	$1\frac{7}{1\frac{1}{2}}$	M., "
Unaltered	1	100 × 2	None	2	F.
	1	100 × 2	"	7	M.
	1	100 × 3	Marked	$2\frac{1}{2}$	F.
	1	100 × 3	Slight	9	M., scarred
	$1\frac{1}{2}$	100	None	33	F., "
	$1\frac{3}{4}$	100 × 2	Not noted	4	M.
	2	100	Moderate	$1\frac{3}{2}$	M.
	2	100 × 2	"	17	F.

TABLE II (continued).

	Duration of treatment (months).	Daily dosage (mg.).	Coloration of skin.	Duration prior to treatment (years).	Sex.
Unaltered	2	$\left\{ \begin{array}{l} 100 \times 3, \text{ 3 weeks} \\ 100 \times 2, \text{ 5}\frac{1}{2} \text{ weeks} \end{array} \right\}$	Slight	18	M., scarred
	2	100 $\times$ 3	"	14	F., "
	2	100 $\times$ 3	Marked	10	M., "
	3	100 $\times$ 2	"	9 $\frac{1}{2}$	M., "
	4	100 $\times$ 2	"	23	F., "
Worse	$\frac{1}{2}$	100 $\times$ 3	Moderate	4	F.
	2	100 $\times$ 2	Slight	3	F.
	2	100 $\times$ 3	Marked	6	F.
	2	100 $\times$ 2	"	2	F.
	4	100 $\times$ 2	Moderate	20	F., scarred

retained by the body might have differed widely because of the different periods of administration. It was therefore thought that skin staining might be a better criterion of sufficient dosage, but this too can be misleading, since a skin adequately stained at first might not be so at a later stage in the course when the dose has been reduced; also it does not necessarily follow that mepacrine is distributed evenly and at the same rate throughout all the tissues. Possibly its beneficial effect is due to its action elsewhere than in the skin; for example, it may have an ACTH-like action. While the majority of those who improved had marked or moderate skin staining, so did the majority of those who did not improve, and there were a few who did well whose skins were only slightly or not at all stained. Statistically, staining is not significant ($\chi^2 = 1.080$; $P = 0.30 - 0.20$). This is also so when only those whose skins were markedly stained are considered as adequately stained ($\chi^2 = 0.127$; $P = 0.95 - 0.90$). An adequately stained skin is not a prerequisite for a good therapeutic response; conditions other than an easily visible amount of mepacrine in the skin must be present before response occurs.

Twenty-six of the 33 patients who were more than slightly improved were questioned about the relationship between the onset of skin staining and improvement. In 21 the staining preceded or was coincidental with improvement, and in 5 improvement came first.

It was hoped that if the total amount of mepacrine administered was calculated some fact of significance might emerge, but this was not so. The fourfold table has been calculated in three ways (the numbers would not allow of further subdivision), and in none of these is P significant.

4.2–10 g. and over 10 g., $\chi^2 = 0.280$; $P = 0.70 - 0.50$.

4.2–12 g. and over 12 g., $\chi^2 = 0.011$; $P = 0.95 - 0.90$.

4.2–20 g. and over 20 g., $\chi^2 = 2.510$; $P = 0.20 - 0.10$.)

PABA (Table III): Here again varying amounts were administered for varying periods, and again the dosage is not the determining factor between

TABLE III.—PABA.

	Duration of treatment (months).	Daily dosage (grammes).	Duration prior to treatment (years).	Sex.
Completely cleared	4	1×3	$1\frac{2}{12}$	F., scarred
	5	1×3	$\frac{1}{12}$	F.
	6	$\left\{ \begin{array}{l} \frac{1}{2} \times 3, 3 \text{ months} \\ \frac{1}{2} \times 2, 3 \text{ months} \end{array} \right\}$	2	F.
Considerably improved	3	$\frac{1}{2} \times 3$	7	F., scarred
	4	$\left\{ \begin{array}{l} 1 \times 3, 2 \text{ months} \\ \frac{1}{2} \times 3, 2 \text{ months} \end{array} \right\}$	17	F.
	4	1×3	5	F.
	6	1×3	12	M.
Moderately improved	6	1×3	11	M., scarred
	8	$\left\{ \begin{array}{l} 1 \times 3, 5 \text{ months} \\ \frac{1}{2} \times 3, 3 \text{ months} \end{array} \right\}$	7	M.
	9	$\left\{ \begin{array}{l} 1 \times 3, 6 \text{ months} \\ \frac{1}{2} \times 3, 3 \text{ months} \end{array} \right\}$	30	F., scarred
	9	1×3	13	F., "
	2	$\frac{1}{2} \times 3$	10 weeks	M.
Slightly improved	6	$\left\{ \begin{array}{l} 1 \times 3, 4 \text{ months} \\ 1 \times 3 \end{array} \right\}$	6	F.
	14	$\left\{ \begin{array}{l} \frac{1}{2} \times 3, 6 \text{ months} \\ \frac{1}{2} \times 2, 4 \text{ months} \end{array} \right\}$	23	M.
	1	$\frac{1}{2} \times 2$	4	F.
Unaltered	1	$\frac{1}{2} \times 3$	6 weeks	F.
	2	$\frac{1}{2} \times 3$	18	M., scarred
	2	1×3	3	F.
	2	1×3	20	F., scarred
	2	1×3	$3\frac{1}{2}$	F., "
	3	$\frac{1}{2} \times 3$	$9\frac{1}{2}$	M.
	3	1×3	$2\frac{3}{4}$	M.
	3	1×3	$6\frac{1}{2}$	F.
	6	1×3	$5\frac{1}{2}$	F.
	6	1×3	2	F.
	9	1×3	5	M.
	1	$\frac{1}{2} \times 3$	1	F., scarred
	3	1×3	23	F., "
Worse	3	1×3	2	F.
	3	1×3	33	F., scarred
	3	1×3	4	F.
	5	$\left\{ \begin{array}{l} 1 \times 3, 3 \text{ months} \\ \frac{1}{2} \times 2, 2 \text{ months} \end{array} \right\}$	17	F.

success and failure. PABA was administered for much longer periods than mepacrine. Those who cleared completely or improved considerably received amounts varying from $\frac{1}{2}$ g. three times daily for 3 months to 1 g. three times daily for 6 months. There was no significant difference between those who received a total amount of 500 g. or under, and those who received over 500 g. ($\chi^2 = 0$; $P = 0.99$).

Type of lupus erythematosus.—The patients have been divided into those whose lupus erythematosus was keratotic, those whose lesions were infiltrated, and the others. In addition, they have been subdivided into those with scarring and those without; this subdivision was made because scarring perhaps indicates a more severe degree of lupus erythematosus.

All types were improved by mepacrine, but one infiltrated in the PABA series was not. This latter fact by itself is meaningless.

Mepacrine was more effective in the non-scarred than in the scarred cases ($\chi^2 = 5.203$; $P = 0.05 - 0.02$), but PABA did not have this selective action ($\chi^2 = 0.051$; $P = 0.90 - 0.80$).

Duration of lupus erythematosus prior to start of treatment.—The duration of the disease prior to the start of treatment was not significant with either mepacrine or PABA.

Mepacrine: 0-2 years and over 2 years, $\chi^2 = 0.110$; $P = 0.80 - 0.70$.

0-5 years and over 5 years, $\chi^2 = 0.269$; $P = 0.70 - 0.50$.

0-10 years and over 10 years, $\chi^2 = 0.583$; $P = 0.50 - 0.30$.

PABA: 0-7 years and over 7 years, $\chi^2 = 1.118$; $P = 0.30 - 0.20$.

0-10 years and over 10 years, $\chi^2 = 2.577$; $P = 0.20 - 0.10$.

The patients have not been classified according to severity, because some were first seen by the author only after they had been under treatment for some time, and because it is difficult to decide whether lupus erythematosus that is infiltrated should be regarded as more severe than that which is, for example, mainly keratotic. It was decided that duration prior to treatment and presence or absence of scarring would give a better idea of severity than a clinical impression.

Patients treated with both mepacrine and PABA.—Eight out of 19 patients failed to respond to either treatment, 4 responded to both, 7 responded to mepacrine after failing with PABA, and none responded to PABA after having failed with mepacrine. This again suggests that mepacrine is more effective than PABA.

Comparison of mepacrine with other treatments.—Treatments, other than PABA, previously used on the 60 patients treated with mepacrine included gold, bismuth, arsenic, vitamin E, sulphathiazole, penicillin, CO₂ snow, antry-pol, thorium x, cortisone ointment, quinine and x-ray.

Seventeen of the 60 (28.3%) had been completely or almost completely cleared with other methods as compared with 27 (45%) with mepacrine. Thirty-nine of the 60 were treated with gold, and 9 of these (23%) were either completely or almost completely cleared as compared with 27 (45%) of the mepacrine patients.

The χ^2 test has not been applied, as not all of the 60 patients received either prior treatment or gold.

Side Effects (Table IV).—All of the side effects encountered were of little consequence apart from lichenoid dermatitis, which occurred in 2 patients treated with mepacrine, and which might well be a more serious disability than the original disease. Both appeared after relatively long courses. The other side effects might cause the patients to cease taking the tablets.

Progress.—*Mepacrine*: Of the 33 patients in the first three categories 13 have just stopped treatment or went directly on to other treatments, and

TABLE IV.—*Side Effects.*

<i>Mepacrine :</i>					
Lichenoid dermatitis . . .	2			Looseness of bowels . . .	1
Generalized itching . . .	2			Epistaxis	1
Nausea	9			Euphoria	2
Malaise	3			Insomnia	1
Vomiting	1			Dizziness	1
Headache	1				
Lichenoid dermatitis occurred after (1) 100 mg. twice daily for 15 weeks.					
(2) 100 mg. thrice daily for 4 months.					
<i>PABA :</i>					
Nausea	1			Vomiting	1

9 relapsed within 2–4½ months of stopping mepacrine. Eight of the 9 relapsed during the summer and 1 at Easter following exposure to bright sunlight. Eleven have not relapsed, but the longest period of observation has been 6 months.

PABA : Three of the 11 patients in the first three categories have ceased treatment or went directly on to another treatment, and two relapsed within 3 and 5 months respectively of stopping PABA. Five have remained clear, but again no patient has been followed up for more than 6 months. One patient did not return for further observation.

DISCUSSION.

Mepacrine.—Page (1951) suggested that the beneficial effect of mepacrine might be due to a light barrier effect, to an ACTH-like effect, or to antagonism of adenylyl groups. In support of the first hypothesis he found that the time required to administer a minimum erythema dose of ultra-violet light was increased after mepacrine had been given for 10 days, and that this returned to normal 10 days after the mepacrine had been stopped. This, he realized, would not account for the improvement that had taken place in patients with disseminated lupus erythematosus, nor could it account for the improvement in the associated arthropathy of another case.

The following points in this study also suggest that part, at least, of the beneficial effect is due to a light barrier effect :

(1) Eight of the 9 patients who relapsed did so in the summer and the other followed exposure to bright sunlight at Easter time.

(2) The only time a very fair-skinned acquaintance was able to expose his skin to sunlight with impunity was when it was heavily stained with mepacrine taken as a malarial prophylactic.

(3) To test the light barrier hypothesis 4 patients with actinic dermatitis were treated with mepacrine. Two patients who received respectively 100 mg. daily for 2 months and 100 mg. three times a day for 1 month were unaltered, but one who received 100 mg. daily for 1 month was completely cleared of her rash, and one who received 100 mg. daily for 3 months was almost com-

pletely cleared. These women had suffered from this condition every summer for 30 and 11 years respectively, and neither had had any relief before.

That skin staining was not of significance in the patients who did well does not necessarily negate this line of reasoning, since only small amounts of mepacrine in the skin might be enough to act as a barrier to light.

The above, however, does not account for the fact that women responded better than men. The reason for this is not apparent in this study.

There was one patient with subacute disseminated lupus erythematosus in this series. Her condition deteriorated during mepacrine treatment but was doing so before it was started.

These patients have not been followed up for long enough, but already it is apparent that there is a moderate relapse rate. Some who might have relapsed may not have done so because their treatment finished in the autumn. A long-term assessment is necessary, but it seems doubtful whether mepacrine will be regarded as anything more than another useful drug in the treatment of lupus erythematosus, likely to produce temporary but not permanent improvement.

PABA.—In 1948 Zarafonitis, Grekin and Curtis reported 18 patients suffering from lupus erythematosus treated with sodium para-aminobenzoate. They were given 2–4 g. of the drug orally every 2–3 hours day and night while in hospital and at longer intervals as outpatients. The majority received 24 g. daily for periods varying from 2 weeks to 9 months. Fourteen were improved in some degree; two with subacute disseminated lupus erythematosus received treatment for 7 and 9 months respectively, during which time their lesions were in remission. The only patient with acute disseminated lupus erythematosus died. A diminution in the amount of round-cell infiltration was noted in 4 patients who had had biopsies performed before and after treatment.

In the discussion that followed the presentation of their paper, Rein reported 13 patients treated with sodium para-aminobenzoate in the same way. He considered the results poor in all cases. In the same discussion Greenhouse reported on 3 patients with acute disseminated and 3 with chronic disseminated lupus erythematosus treated in the same manner. Two with the disseminated disease died and the other recovered. All 3 with the chronic form improved.

In the following year Grekin and Zarafonitis (1949) reported on another 12 patients similarly treated with comparable results.

Vilanova and De Dulanto (1951) treated a patient with subacute disseminated lupus erythematosus, in whom L.E. cells were demonstrated both in the peripheral blood and bone marrow, with sodium para-aminobenzoate. This person's condition improved rapidly and the L.E. phenomenon disappeared.

None of the authors offered any explanation of why PABA should be effective in this disease. Zarafonitis and his colleagues originally used it because

some relapses were known to be due to sunlight and because some examples of actinic sensitivity were known to have followed the administration of sulphonamides or allied compounds. Since PABA and sulphonamides are metabolic antagonists they thought it might be of benefit. PABA applied locally definitely acts as a barrier to light (Rothman and Rubin, 1942), but there is no definite evidence that when given orally it has this action. Zарафонетис tested 9 patients before treatment, and found that the erythema dose of ultra-violet light was less than normal in 5. The only one tested after treatment was found to be less sensitive.

SUMMARY.

(1) Sixty patients with lupus erythematosus were treated with mepacrine and 32 with PABA.

(2) Mepacrine was more effective than PABA when all degrees of improvement were recorded, though this was doubtful if clearance or major improvement alone were considered.

Women responded better than men to treatment with mepacrine.

Mepacrine was more effective in patients showing no scarring. This was not so with PABA.

The duration of the disease before treatment was not significant with either mepacrine or PABA.

The total amount of mepacrine administered was not a determining factor in those patients who responded well to mepacrine.

There was no significant difference in the results of those who received a total dose of under 500 g. of PABA and those who received over 500 g.

Skin staining was not a significant factor in those who did well with mepacrine.

In the absence of a control series of patients or a generally accepted spontaneous cure rate it cannot yet be stated with assurance that either drug is therapeutically effective.

(3) Part of the effectiveness of mepacrine is probably due to a light barrier action.

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SYSTEMIC LUPUS ERYTHEMATOSUS WITH NODULAR LESIONS :

Report of a Case.

A. N. P. MILNER, M.D.

THE following case displayed three unusual concomitant features : generalized lymphadenopathy of sudden onset which preceded the dissemination of the skin lesions, polyserositis, and a skin eruption in which nodular lesions were mingled with the typical skin lesions of lupus erythematosus.

CASE REPORT.

An unmarried blonde female aged 22 was admitted to hospital on 28 October 1949.

History.—The skin eruption began in March 1949 with redness and slight swelling of the upper eyelids associated with soreness and burning sensations aggravated by wind, cold and sunlight. This failed to respond to a variety of local applications.

Seven days before admission the lymph nodes in the groins, axillae and sides of the neck became enlarged, and at the same time a sense of fullness and discomfort was felt in the upper abdomen. The latter increased so that she now complained of abdominal swelling, soreness, anorexia, constipation and flatus dyspepsia accompanied by lassitude and general malaise.

Three days before admission new skin lesions appeared on the face, neck, fingers, toes, and arms ; the joints of both wrists became painful to move, slightly swollen and tender to touch.

Past history.—At the age of five years a purulent ear discharge followed measles. This persisted with remissions and exacerbations for seven or eight years and then disappeared. Three years ago this discharge returned and had persisted in some degree ever since.

In September 1943 she was admitted to another hospital with symmetrical swellings on the dorsal surfaces of the wrists. Case note : " There is a ganglion on the dorsum of left wrist and fluid effusion into right wrist joint ". The wrists were put up in plaster for 3 months.

At operation (11.xii.43) " a mass of granulation tissue was removed from the extensor tendons of the left wrist." The pathologist reported " granulation tissue with chronic inflammatory changes. It does not reveal any specific histology." Sedimentation rate and blood W.R. were reported normal. Operation on the right wrist two months later revealed the same condition.

In summer 1947 she was admitted to a third hospital with recurrence of pain and swelling of both wrists. Skiagrams revealed " a picture which would do equally well for mild, chronic tuberculous disease or chronic rheumatoid arthritis". Mantoux test and skiagram of chest were negative. Case note : " the weight of evidence is against tuberculosis and in favour of rheumatoid arthritis." Treatment with twelve weekly injections of Myocrisin cleared up the joint swellings.

Condition on admission.—The skin eruption included lesions of the following types : pinkish-red slightly elevated oedematous patches with a bluish tinge covering the upper eyelids ; lesions of a similar type on the lobes of the ears, the exposed V-shaped area of the premanubrial part of the chest and on the adjacent parts of the neck ;

pinkish-red more sharply defined plaques and patches of small size with prominent follicular orifices on the malar eminences; bluish-red ill-defined macular telangiectatic lesions on the dorsal surfaces and tips of the palmar surfaces of the terminal phalanges of most of the fingers and toes.

In addition to these were lesions of an unusual type consisting of bluish-red raised nodules varying from 1.5 to 2.5 cm. in diameter, situated in greater part deeply in the cutis, and bearing a superficial resemblance to sarcoid lesions. They were grouped symmetrically on the lateral parts of the face, extending from the lateral hair margins to the angle of the jaw and also on to the anterior surface and lower margin of the chin. On the antero-lateral surfaces of both arms, near to the elbows, there were tumorous lesions extending deeply into the skin. They presented rounded swellings of a bluish-red mottled appearance not sharply outlined, firmly adherent to the skin and freely movable with the skin on the underlying structures.

Movements were limited and painful in the right shoulder and in both wrist joints, which were tender to touch; the latter were distended with fluid. On the dorsal surfaces of both wrists were the scars of surgical incisions. The lymph nodes of the anterior and posterior triangles of the neck, of the axillary, inguinal and femoral groups and the epitrochlears were enlarged; some of the glands of the neck were as large as damsons. The parotid glands appeared to be normal in size and consistency. There were no eye changes. The right lobe of the thyroid gland was slightly enlarged.

Heart and lungs appeared normal to physical examination, pulse 88, B.P. 130/80, respirations 30, temperature normal (this later showed evening rises to 99° F. and morning remissions to 97° F.). There was a small amount of sero-purulent discharge from the right external auditory meatus and the right tympanic membrane showed an old-standing posterior marginal perforation; mastoid not tender. The abdomen was slightly distended, and some degree of tender, doughy resistance to palpation was present in the epigastrium. The tip of the spleen was just palpable.

Investigations.—Blood W.R. and Kahn tests negative; E.S.R. 33; Blood group A; Rhesus +.

The following investigations were all normal: blood count, blood urea, blood cholesterol, non-protein nitrogen, plasma proteins and A/G ratio, serum calcium, acid and alkaline phosphatase; skiagrams of lungs, small bones of hands and feet and paranasal sinuses.

Culture of nasal swab: scanty growth of non-haemolytic staphylococci. Culture of throat swab: moderate growth of *Str. viridans* and scanty growth of monilia.

Mantoux test: negative 1 in 100,000; positive 1 in 10,000; strongly positive 1 in 1000; there were no focal reactions.

Urine; trace of albumin; centrifuged deposit normal; culture sterile.

Histology.—(Dr. I. Muende). Tumour lesion of left arm: "Skin section shows all the characteristics of lupus erythematosus." Gland removed from neck: "Gland shows simple chronic irritative changes."

Course.—During the first twelve days after admission the swellings and tenderness of the wrists increased and the right shoulder became swollen. The abdominal distension and discomfort increased and aerophagy became almost continuous, leading to nausea, vomiting and progressive anorexia. The general condition deteriorated slowly but steadily.

On 11.x.49 an elliptically shaped tumour was noticed in the mid-line of the back extending over the distal thoracic and proximal lumbar vertebrae. It was 18 cm. long, 5.5 cm in its widest diameter and 2 cm. high at the same level, from which it shelved down towards the level of the skin at its proximal, distal and lateral borders. It had a bluish-red stippled surface, firm in consistency and was situated in the skin, with which it could be moved freely over the underlying structures.

On 12.x.49 the right ear became swollen and painful and developed a copious purulent discharge. The E.N.T. surgeon reported chronic mastoiditis and advised

a radical mastoid operation when the general condition had improved. Culture of pus: *Proteus vulgaris*.

On 20.x.49 three small tumours, similar to those on the arms, appeared on the right side of the chest and on the interscapular region; a patch of L.E. appeared on the left buccal mucosa.

On 31.x.49 the patient complained of pain in the chest and was found to have a bilateral pleural effusion, which was confirmed by skiagram.

During November 1949 additional nodules appeared on the arms, dorsal surfaces of the elbows and anterior surfaces of the arm flexures. The abdominal distension and ascites increased rapidly and the patient took less and less food. The temperature which up to this time had ranged between 97° F. and 99.6° F., rose to 101° F. and remained continuously above normal with a range from 99° F. in the morning to 101° F. at night and her general condition deteriorated rapidly. On 18 November 1949 laparotomy was performed in an attempt to relieve the abdominal distension and associated symptoms. More than a gallon of ascitic fluid was removed. The right kidney was found to be enlarged, the spleen more than twice normal size and bound down by adhesions, the peritoneum congested and oedematous, the colon slightly distended and the upper abdominal lymph glands slightly enlarged; the liver and small bowel appeared normal. The ascitic fluid contained a moderate number of cells (lymphocytes 96%, polymorphs 4%). Cultures: sterile and T.B. negative; guinea-pig inoculation for T.B. negative.

From 19 November until her death on 5 December the patient maintained a continuous mild pyrexia. During the last 44 hours of life the temperature rose to 104° F. and for the last 8 hours was maintained at 105° F.

At the time of death the skin lesions on the face, hands and feet were much the same as on admission, but the nodular and tumour lesions of the trunk and arms had increased both in number and size. The latter numbered fifteen in all, and were distributed on the distal parts of the arms, the dorsal surfaces of the elbows, the sides of the chest, interscapular and thoraco-lumbar areas of the back and on the occipital region. The ascites recurred after laparotomy, and the wrist and shoulder joints remained distended with fluid up to the time of death.

Treatment.—Intensive courses of penicillin were given with little effect; streptomycin was tried but not tolerated; sulphatriad in 1 g. doses four times daily and calciferol 50,000 units up to four times daily were also tried in conjunction with penicillin. No treatment was of any real service. The nausea, aerophagy and vomiting associated with ascitic distension made it almost impossible to give drugs effectively by mouth.

Post-mortem examination was made by Dr. M. Corridan, who reported as follows:

Right ear and mastoid showed chronic otitis media and destruction of the mastoid cells, which were replaced by inspissated pus and cell debris.

Skin: On the face several patches and nodules of L.E., small tumours on the trunk, scalp and upper limbs and an elliptical tumour 18 cm. by 5 cm. over the lower thoracic vertebrae.

Thoracic cavities: The pleural cavities contained 4 pints of clear yellowish fluid. The pleurae were thickened and adherent to the lower lobes of the lungs, which were collapsed.

Heart and pericardium: The pericardium appeared normal, but the cavity contained an excess of clear yellow fluid. Heart weight 16 ounces (455 g.) Left ventricle hypertrophied and dilated; the wall at its greatest diameter measured 2.5 cm. Several flat, whitish vegetations were present at the junctions of the anterior and posterior cusps of the mitral valve with the auricular endocardium, on to which they extended for a distance of 1 cm. There were large flaky patches of fibrin on the surface of the mural endocardium of the left ventricle. A few flat vegetations were present on the right cusp of the aortic valve, which extended from its base for a few

centimetres on to the ventricular endocardium. Similar vegetations were also present on the tricuspid valve at the junction of its base with the auricular endocardium.

Abdominal wall was oedematous and there was marked gelatinous oedema of mesentery, peritoneum and posterior abdominal wall. The cavity contained ten pints of clear yellowish fluid. *Liver* weighed 64 ounces (1820 g.) and its surface had a greasy appearance. The *spleen* weighed 10 ounces (285 g.) Its capsule was thickened and showed gelatinous adhesions. The cut surface of the spleen was dark red and fairly firm. *Kidneys* were both enlarged; the right weighed 10 ounces (285 g.) and the left 12 ounces (342 g.). Their capsules stripped easily, displaying a mottled red and white surface with normal pattern. There were dark pin-point areas of glomerular haemorrhages in the cortex. The pelves of the kidneys, the ureters and bladder were normal. *Uterus and ovaries* were normal. *Stomach* normal.

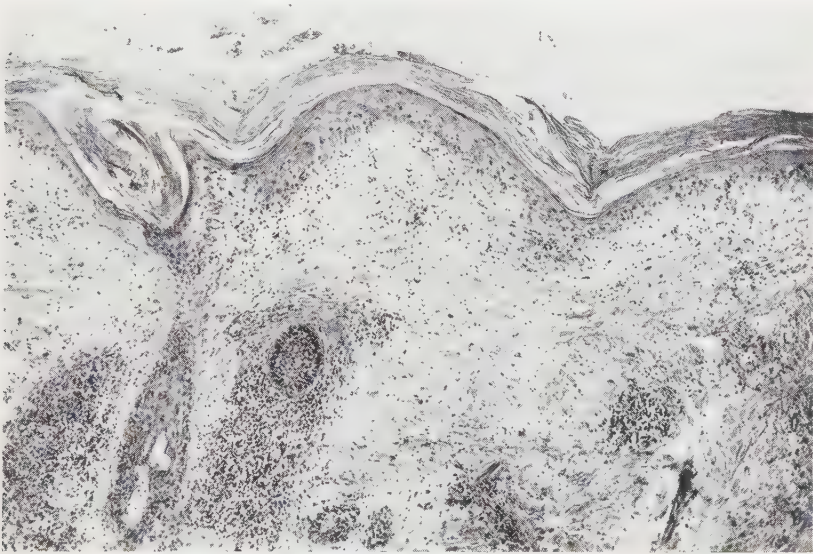


FIG. 1.—Skin section from a small tumour of the arm. Note keratotic plugging of follicles with atrophy of the epidermis and inflammatory infiltration of the dermis. H. & E. $\times 60$.

Intestines showed some recent adhesions. *Thyroid gland*: Left lobe small and atrophied; right lobe hard, fibrous and slightly reduced in size. Histology showed increased interstitial fibrosis. Weight of gland 0.6 ounces (17 g.).

Histology of lymph gland showed fibrinoid necrosis of the capsule, greatly congested and numerous blood vessels and absence of follicles; hyperplasia of the reticulo-endothelial cells, and plasma-cell and basophilic mononuclear-cell infiltration.

Histology of the large tumour of the back. Hyperkeratosis and plugging of the follicles by masses of keratin (cf. Fig. 1); marked degeneration of the collagen and elastic fibres of the corium; degenerative changes in the walls of the vessels of the subpapillary area, which were dilated. In the deeper parts of the corium there was myxomatous degeneration, thrombotic occlusion of the vessels and some polymorphonuclear-cell infiltration.

Histology of post-mortem material was reported upon by Dr. Ian Rannie as follows:

Kidney: In the immediate subscapular zone there is tubular atrophy with replace-

ment fibrosis and round-cell infiltration. The glomeruli are, for the most part, normal, and only an occasional glomerulus shows the so-called wire loop change (Fig. 2). The tubules in the deeper cortex show considerable degenerative changes

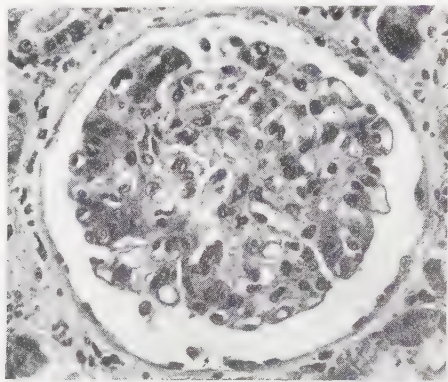


FIG. 2.—Renal glomerulus showing wire-loop change. H. & E.



FIG. 3.—Vegetation on ventricular surface of the mitral valve. The dark masses are composed of haematoxylin bodies. H. & E. $\times 9$.

with fat droplet accumulation. An occasional recent thrombus is found in the smaller arteries but the afferent and efferent arterioles are normal.

Heart: The ventricular surface of the base of the mitral valve and the adjacent ventricular endocardium are covered by recent vegetations with commencing organization (Fig. 3). In the thrombus are many clumps of characteristic haematoxylin bodies typical of disseminated lupus erythematosus (Fig. 4). The myocardium

shows interstitial oedema; in its arterioles there are many recent thrombi, some of which show commencing organization and haematoxylin bodies. There is a small amount of fibroid change in the collagen but there are no collections resembling Aschoff nodes.

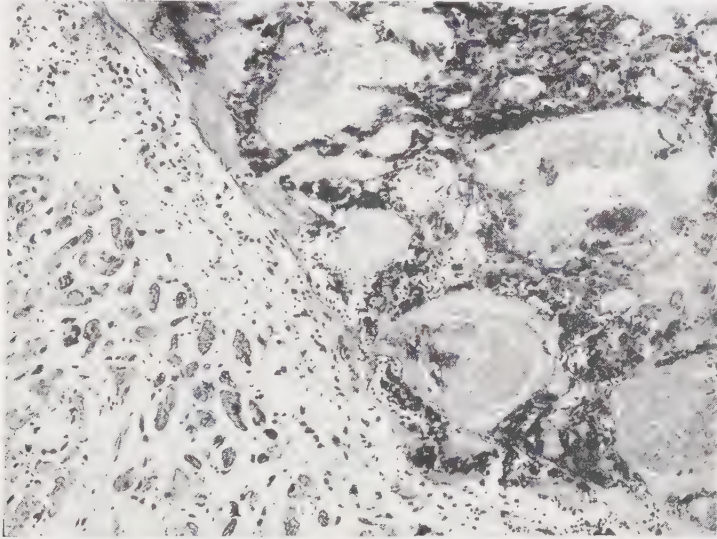


FIG. 4.—Portion of vegetation on ventricular wall showing the "haematoxylin bodies" as dark masses in the interstices of the thrombus. H. & E. $\times 125$.

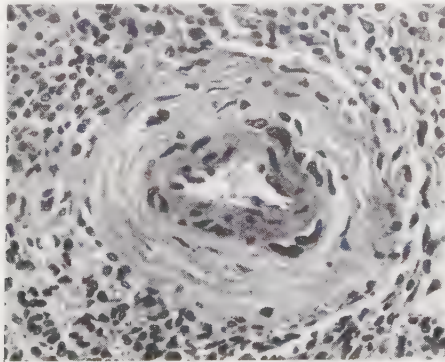


FIG. 5.—Splenic arteriole, concentrically thickened. H. & E.

Spleen: The capsular surface shows a partially organized fibrous exudate. Malpighian bodies are small, and represented in most instances by a mere rim of lymphocytes. The arterioles show marked perivascular fibrosis (Fig. 5), and occasionally the lumen is occupied by a hyaline thrombus.

Lung: Collapse and an almost completely organised fibrous pleurisy.

DISCUSSION.

I have not been able to find a description of a case similar to the above.

The deep-seated nodular and tumour-like lesions in my case conform, more or less, to those described by Ormsby and Montgomery (1943) under the title of lupus erythematosus profundus as "a deep nodular form in which the lesions resemble Darier-Roussy sarcoid and erythema induratum." But these authors classify this variety as one of the chronic forms of the disease; they do not mention it as one of the possible manifestations of systemic lupus erythematosus.

The variant described by Bechet (1950) under the title lupus erythematosus hypertrophicus et profundus does not appear to correspond to my case in any way, and this again is classified as a variant of the chronic form of the disease.

Radcliffe-Crocker (1893) credited Kaposi with describing lesions occurring in lupus erythematosus as "subcutaneous, deeply seated, doughy, painful and tender nut-sized nodules (which) appear while the skin over them is still normal." All the deeply-seated lesions in my case were attached to the overlying skin which exhibited a stippled bluish-red discoloration. Radcliffe-Crocker also classifies these with the chronic forms of the disease.

The technique for demonstration of L.E. cells had not been developed in this area, and cortisone and ACTH were not available for treatment at the time this case came under my care.

Although the Mantoux test was positive, tuberculous foci could not be demonstrated either clinically or at post-mortem.

The chronic mastoiditis may have acted as a toxic focus influencing the disease. Unfortunately, ante-mortem swab cultures were not helpful, and post-mortem culture of the mastoid debris was not carried out.

After transfusion with one pint of whole blood from a donor convalescent from an attack of disseminated discoid L.E. and otherwise suitable, the patient produced her first definite though mild pyrexial reaction, which was then maintained until death. It is not clear whether this has any significance.

The skin eruption consisted roughly of three varieties of lesions: the typical more superficial lesions of L.E. distributed on the eyelids, malar eminences, sides of the neck and V-shaped exposed area of the chest and the dorsal surfaces of the distal phalanges of the fingers and toes; the sarcoid-like lesions on the sides of the face and chin; the larger group, consisting of nodules and tumours of various sizes which were distributed irregularly on the arms, trunk and scalp. The first two groups remained stationary in size, number and appearance from the time of admission until death; the nodular and tumour-like lesions began as small-sized nodules which increased to various sizes and also multiplied; they all produced the same bluish-red discoloration of the skin to which they were attached. All the nodules and tumours appeared as

discrete lesions and remained so; the larger tumours grew from originally small ones; in none was there confluence of two or more tumours.

SUMMARY.

A case of systemic lupus erythematosus is described which displayed the typical skin lesions of this disease and also multiple skin nodules and swellings, combined with ascites, polyserositis and general lymphadenopathy. Post-mortem examination revealed visceral lesions which conformed to those described by Libman and Sacks (1924), Baehr, Klemperer and Schifrin (1935), and Klemperer, Pollack and Baehr (1941).

I wish to record my indebtedness to the pathologists, Drs. Ian Rannie and M. Corridan, for the post-mortem and histological reports, to Mr. E. Travers for surgical assistance, and to Dr. F. K. Storrington for the microphotographs.

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AN UNUSUAL ALOPECIA CAPITIS IN ACUTE LUPUS ERYTHEMATOSUS, SCLERODERMIA, AND DERMATOMYOSITIS.

CLIFFORD D. EVANS.

A CURIOUS type of scalp alopecia has occurred in two cases of acute disseminated lupus erythematosus, one of chronic lupus erythematosus with progressive symmetrical sclerodermia, and one of dermatomyositis. The baldness is most marked in the temporo-frontal area and is accompanied by a profuse dry greyish scaling of the whole scalp. All the scalp hair is lost in a few weeks and later regrows.

This condition is reported as no previous similar cases appear to have been recorded in the literature.

CASE REPORTS.

CASE 1.—*Acute disseminated lupus erythematosus.*—A woman aged 33.

In June 1949 the patient developed a red, dry scaling of the face made worse by exposure to sunlight. In January 1951 she was admitted to hospital with pericardial and bilateral pleural effusions and she was desperately ill. A blotchy erythematous rash was present affecting chiefly the face, front of the chest, backs of the hands and fingers, and the upper surfaces of the toes and feet. The scalp was covered by fine grey scales. A few hairs, about a quarter of an inch long, were scattered over the frontal area, with a fringe of hair half an inch long at the hair margin. The remainder of the scalp was sparsely covered with hairs of normal length.

Investigations.—Repeated blood sedimentation estimations were between 40–60 mm. in the first hour. The serum protein was raised, with a reversed albumin-globulin ratio. There was a persistent anaemia with relative leucopenia. The 17-ketosteroids were 2 mg. in 24 hours. Hargraves's L.E. cells were isolated from the buffy layer of the blood.

Progress.—She was placed in an oxygen tent and given daily penicillin injections, with gradual improvement. The hair over the whole scalp was shed, gradually regrew, and the scaling disappeared before she was treated with ACTH, starting on 8 March. The dose was varied between 75 mg. daily in one dose and 12.5 mg. twice daily, the whole course lasting 7 weeks. Euphoria occurred, but there was little clinical improvement. While she was having this treatment she developed facial pigmentation and an acute throat infection, as well as multiple infected skin lesions of the fingers and face. At the end of June she developed a lung abscess and her condition continued to deteriorate. Congestive heart failure supervened, and she died on 8 August 1951.

Post-mortem.—Glomerular thromboses were present, but no other lesions of disseminated lupus erythematosus were found.

CASE 2.—*Acute disseminated lupus erythematosus.*—A woman aged 24. She was a diabetic having insulin treatment.

In September 1949 she was admitted to hospital with a five months' history of an erythematous rash starting on the forehead and spreading to the ears, bridge of the nose and cheeks. Three weeks before admission she had noticed lassitude and generalized aches and pains.

There was a scaly erythema of the forehead extending to the ears and also involving the butterfly area of the face; similar lesions were present on the dorsal surface of the hands and fingers. She had stiffness of all the limbs and her muscles were tender on pressure. The temperature was 100° F.

Investigations.—Blood sedimentation rate 60 mm. during the first hour. The blood count revealed a leucopenia of 2200 white cells with 55% polymorphs and no eosinophils, but was otherwise normal. The serum protein was above normal and the albumin-globulin ratio reversed. Fasting blood-sugar 0.297%. Urinary 17-ketosteroids 1.5 mg. per day. Hargraves's L.E. cells were demonstrated in the buffy layer of the blood.

Progress.—Shortly after admission she noticed that her scalp hair was falling and it quickly became thin all over. The temporo-frontal area was almost completely bald except for a thin fringe of hairs about half an inch long at the hair margin. Gradual regrowth of the hair over the whole scalp occurred during the next few months.

The patient developed pericarditis with effusion in December 1949 and bilateral pleural effusion in January 1950. In February she was given a three weeks' course of ACTH, 100 mg. daily for one week, 50 mg. daily for the next week, and 25 mg. daily for the third week, when supplies were exhausted. Within 24 hours of commencing ACTH treatment there was a dramatic symptomatic improvement in the patient's condition; she had been semi-comatose, but became bright and took an interest in her surroundings. During the course of this treatment she gradually relapsed as the dose was reduced.

The skin lesions improved slowly from the time of admission and had almost disappeared when she died in April 1950.

Post-mortem.—The chief feature was a pericardial effusion of 1½ pints of haemorrhagic exudate with mucoid brownish pus freely mixed with it. The epicardium showed adherent shaggy brownish exudate. The heart was compressed by the exudate but no valvular disease was present.

CASE 3.—*Chronic lupus erythematosus with progressive symmetrical sclerodermia.*—A woman aged 38.

In February 1950 she was admitted to hospital with discoid lupus erythematosus affecting the butterfly area of the face and also the scalp. The rash had started two years previously, and a year later she had developed arthritis of the feet and hands, with spindle-shaped swellings of the finger joints. The chief clinical findings were pyrexia up to 103° F. soon after admission, a normochromic, normocytic anaemia and a reversal of the albumin-globulin ratio of the plasma proteins. The temperature settled and she was discharged from hospital a month later.

She was readmitted to hospital in February 1951, and said that her condition had begun to deteriorate following an attack of pneumonia in June 1950, when her fingertips became infected. There was a well-marked sclerodermatous thickening of the skin of the face with mask-like facies, and of the fingers, which were infected and gangrenous at the tips. The discoid lesions of lupus erythematosus on the face and scalp were healing with scarring. There was a diffuse thinning of the hair of the scalp with almost complete alopecia of the temporo-frontal region, except for a fringe of hairs about half an inch long at the hair margin. The temperature was normal. The spleen could be felt enlarged one inch below the costal margin.

Investigations.—Blood sedimentation rate 50 mm. during the first hour. Blood count showed a normochromic, normocytic anaemia with haemoglobin of 83%. These findings varied little during her six months' stay in hospital. 17-ketosteroids were 2.8 mg. in 24 hours. No Hargraves's L.E. cells were found in the sternal marrow.

Progress.—She was treated with ACTH in doses varying from 100 mg. daily to 6.25 mg. daily for two months. After fourteen days' rest from the drug it was then continued for another four months, starting with 25 mg. daily, and after one month

gradually decreasing to 3 mg. daily. No dramatic effect was noticed with this treatment.

The fingers slowly improved whilst in hospital, and when she was discharged in August 1951 the tips of the fingers were clean with loss of tissue due to gangrene. The scleroderma and sclerodactyly were unchanged. The hair regrew whilst in hospital.

CASE 4.—*Dermatomyositis*.—A woman aged 55.

In October 1951 she noticed stiffness and weakness of the legs and arms. This spread to involve other muscles and she was soon unable to get up from the kneeling position. A fortnight later a red irritating rash appeared on the hands, face and limbs, with scattered patches on the trunk. The rash on the face was accompanied by swelling of the lower eyelids. She was admitted to hospital on 12 December 1951.

There was marked generalized muscle weakness; she could not raise her head from the pillow or sit up in bed. Slight puffiness of both lower eyelids was present. A streaky erythema was seen on the face, neck, arms, backs of the hands, and also to a less extent on the legs. It was profuse on the hands, especially over the joints, and longitudinal haemorrhages were present in the skin at the bases of the nails. She had a diffuse thinning of the scalp hair associated with scaliness. Shortly after admission there was loss of hair in the temporo-frontal region, except at the hair margin in front, where there was a fringe of hair half an inch long (Fig. 1.). A low-grade pyrexia was present and persisted for many weeks. Physical examination revealed no other abnormality except hypertension.

Investigations.—Blood count: W.B.C. 10,500 with 17.5% eosinophils; no other abnormalities. Urinary creatine: 128 mg.%. Total in 24 hours = 0.66 g. 17-ketosteroids 1.8 mg. per diem.

Histology (muscle).—Scattered areas in which the muscle fibres stain poorly and cross striation is absent. Areas of lymphocytic infiltration between the muscle fibres.

Progress.—She was given 3-hydroxy, 2-phenyl cinchoninic acid 500 mg. twice daily for fifteen days without noticeable change in the clinical condition. All the scalp hair was lost, the scaling disappeared and hair regrew about four weeks after the total hair fall. On 22 February 1952 a course of ACTH therapy was started, 200 mg. daily for four days, 100 mg. for four days and 50 mg. for the next eleven days. No clinical improvement was noted during or after this treatment, although she experienced the euphoria commonly associated with the administration of this hormone. She slowly became weaker, developed dysphagia and died. No post-mortem examination was allowed.

DISCUSSION.

In each of the cases here reported the sequence of events has been the same. Early in the course of the disease there was loss of hair in the temporo-frontal region of the scalp which occurred in 10–14 days, causing a curious and characteristic picture (Fig. 1). Before this peculiar alopecia the whole scalp became covered with dry, grey, fairly thick scales, some of which were attached loosely to the hairs. At the same time there was a diffuse defluvium capitis. The bald area at the front of the scalp was covered with short hairs broken off about a quarter of an inch from the epidermis, except at the periphery, where a fringe of hairs half to three-quarters of an inch long was present. About one month after the commencement of the defluvium capitis there was complete alopecia and the scaling slowly disappeared, leaving a smooth bald scalp

in which the hair follicles were easily seen. Removal of the scales in the early stages with keratolytics and shampooing was quickly followed by unsealing as soon as the treatment was stopped. Regrowth of hair occurred soon after the total baldness and was complete over the whole scalp.



FIG. 8.

This curious baldness of the front of the scalp was quite unlike that associated with toxæmia, which affects the whole scalp; it was also unlike the male type of alopecia associated with excess of androgens in both sexes in which the hair recedes in the temporo-frontal regions but leaves a central tuft of hair between the bald areas.

It is interesting that all four cases had a low 17-ketosteroid excretion and all suffered from closely related collagen diseases.

I wish to thank my colleague, Dr. R. P. Warin, for allowing me to include Cases 1 and 3, which were under his care.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. G. B. DOWLING.

16 October 1952.

Case for Diagnosis. ? White Sponge Naevus of the Mouth.—Dr. R. P. WARIN.

E. P. S—, male, aged 24.

History.—Condition first noticed at about 5th year of age. It has never cleared but improved on one occasion when fasting during an “influenza” attack. Worse after spiced or acid foods.

Family history.—One brother aged 21. No similar condition in the family.

On examination.—White, macerated appearance of the inner aspects of the lips, dorsum and sides of the tongue, hard palate, and over the cheeks opposite the line of closure of the teeth. The superficial layers of the white membrane can easily be scraped off but the deeper layers separate with difficulty and leave a raw, bleeding surface.

Investigations.—Blood W.R. and Kahn negative. Scrapings showed no monilia. Histological examination: Hyperkeratosis and parakeratosis. Moderate infiltration of the dermis with neutrophil and lymphocytic leucocytes.

Treatment.—A course of vitamin A in high doses for two months had no effect.

Comment.—Chronic moniliasis is difficult to disprove in spite of negative scrapings. However the condition seems to be very similar to that described by Cannon (1935) as “White sponge naevus of the mouth.” His case also had lesions in the vagina and rectum and had a well marked family tendency. Ludy and Shirazy (1941) described another case under the title “Leukokeratosis mucosa oris,” and in this case, too, there was a family tendency.

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Dr. M. SYDNEY THOMSON: It seems to me this must be naevoid; the curious patches running in streaks reminded me of ichthyosis hystrix which behaves as this mouth lesion behaved in its gradual spread and variation in intensity.

Dr. J. E. M. WIGLEY: Has a monilial infection of the lung been excluded or an X-ray taken?

Dr. R. P. WARIN: A skiagram of the lung has not been taken but we will have it done. He has had the condition for twenty years and there have been no symptoms of lung infection. Even if monilia is demonstrated it would not necessarily indicate it was playing a primary role since if the condition were fundamentally naevoid it would be the sort of field on which monilia likes to grow.

Poikiloderma Congenitale (Thomson).—Dr. C. H. WHITTLE.

H. D. G—, girl, aged 3 years.

History.—Pin-head vesicles and some patchy erythema came on the face and hands at 2 days old. Sunlight appeared to bring out the rash which cleared in the winter. Vesiculation has ceased. The child was 5½ lb. at birth and has never developed properly.

10.xi.50: When first seen the face showed a red mottled pattern on the cheeks suggesting poikiloderma and some erythematous patches on the dorsa of the hands.

Family history.—Father had infantile eczema. Mother's sister suffers from asthma. Brothers aged 3½ years and 9 months are normal.

Present condition.—There is a vermilion reticulate pattern of telangiectasia on the cheeks with a faint suggestion of "glazing" and an occasional scaly or horny patch. The hands and shins show fading patches of erythema. The mother states that sun does not now seem to affect the skin. The child is still microcephalic, grossly undersized and mentally backward. There are no gross keratoses. The shape of the face is somewhat triangular with the apex at the chin.

Blood vitamin A.—22.vi.51: Carotenoids 116 i.u./100 ml. Vitamin A 75 i.u./100 ml. 1.x.52: Carotenoids 111 i.u./100 ml. Vitamin A 65 i.u./100 ml.

Comment.—It is interesting to note that two of Thomson's original (1936) cases showed microcephaly and one was "small and puny" from birth. These features were also noted by Rook and Whimster (1949) in their review of Dowling's case (1931). Other dystrophies occur such as bilateral cataracts and dental defects. Mild xeroderma was noted by Thomson in one case and by Rook and Whimster in theirs. Mild xeroderma was present in the second of two cases published by me (1947). The blood vitamin A was low in both my patients, 45 i.u. and 65 i.u./100 ml. in one, 85 i.u. in the other, as compared with 75 i.u. and 65 i.u. in this case. The syndrome would therefore appear to include the tendency to other maldevelopments and possibly a disturbance of vitamin A metabolism.

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Dr. M. SYDNEY THOMSON: I think this is a typical example of the condition. A point which has always impressed me is the disproportion in the ossification of the cartilage and membranous bones of the skull.

The PRESIDENT: A case under my care, when I first saw her at the age of about 20, showed the vascular change in the face seen in Dr. Whittle's case, a scaly xeroderma-like alteration of the skin of the arms and legs, the characteristic small skull and features, as well as a large number of keratoses situated chiefly on the forearms and legs. Histological examination of these keratoses at that time revealed no sign of malignancy. However, some years later she developed a large epithelioma on the right ankle and this eventually led to amputation of the limb. Since then others have developed malignant change and recently metastases have occurred in regional glands. This seems to be the probable fate of at least some of these cases in adult life. The case has been fully reported by Rook and Whimster.

Dr. C. H. WHITTLE: I should like reassurance that these vitamin A figures are below normal. The normal standard seems to vary so much between one country and another and from year to year.

Dr. A. D. PORTER: They are certainly lower than the ordinary figures for England. Leitner and Moore (1946) found the average figure in hospital out-patients suffering from common diseases of the skin to be 120 i.u./ml. Less than 80 i.u./100 ml. is certainly low.

Miliary Lymphocytoma of the Face.—Dr. E. WADDINGTON.

Mrs. M. K—, aged 42.

History.—July 1951 the eruption began suddenly on the lateral aspects of both cheeks, and new lesions have gradually developed on the malar regions and forehead. The condition remained unchanged until a month ago when some of the spots on her forehead disappeared spontaneously.

She lived in New Zealand and Australia until eighteen months ago and has always spent considerable time in the open air. The eruption occurred after she had been in this country for two months; she does not think it followed sunburn.

Previous history.—1941: Dengue fever. May 1952: Operation for removal of lutein cyst of the ovary.

On examination.—A symmetrical eruption on the forehead, malar regions and pre-auricular areas of the cheeks extends down towards the chin. The lesions are discrete papules varying in size from a pinhead to 3 mm. in diameter. The larger

lesions are reddish-brown in colour, the smaller are semi-translucent and resemble sago grains. All show opalescence on diascopy. There is no scaling. The rest of the skin and mucous membranes are not involved. There is no lymphadenopathy and the liver and spleen are not palpable.

Investigations.—Blood count normal.

Histology (Dr. I. W. Whimster).—The section shows parts of three sharply circumscribed, discrete, dermal nodules of tightly packed, fairly evenly mixed large and small reticulum cells, "lymphoblasts" and lymphocytes, together with an occasional eosinophil. The appearances are those of a "benign light-sensitive lymphoma."

Comment.—This condition was first described by Jadassohn in 1906 as pseudo-leukaemic infiltration of the skin; but in 1921 he reported that his patient never developed signs of leukaemia, although the lesions had been present for thirty years.

The name lymphocytoma was first used in 1921 by Kaufmann-Wolf and similar lesions have been recorded under diagnoses such as localized forms of Spiegler-Fendt sarcoïd, lymphadenosis benigna cutis and benign lymphadenoid granuloma.

There is considerable difference of opinion about the aetiology.

In Europe it is regarded as a benign reaction of lymphoid tissue in response to various stimuli. In 1939 Hallam and Vickers, and in 1943 Bafverstedt, came to the conclusion that in all proved cases malignant degeneration never occurred.

At the International Congress in 1952 Bafverstedt produced evidence that it may occur as a symptom of malignancy elsewhere in the body. He reported 3 cases in association with carcinoma of the oesophagus, a squamous-cell epithelioma of the skin, and dermatofibrosarcoma protuberans.

On the other hand, American authors are not yet decided that it is entirely benign, and this difference of opinion arises from the difficulty in interpreting the histological changes. Two types are described. In one, the infiltrate forms discrete nodules, and in the other, it is diffuse. Both types may, or may not, show the formation of germ-centres and Loveman and Fliegelmann (1951) point out that it is sometimes impossible to distinguish the diffuse type without germ-centres from a malignant lymphoma.

Although a final decision can only be made after prolonged follow-up of all cases, the evidence at present is more in favour of the belief that miliary lymphocytoma is a benign reactive hyperplasia of pre-existing lymphoid tissue. This peculiar reaction occurs in response to irritation of the skin by such varied stimuli as sunlight, minor trauma and even insect bites.

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Dr. I. W. WHIMSTER: The cases we have had at St. Thomas's which belong to the broad category of "lymphocytoma" fall into two distinct groups, both on their histology and on their natural history.

In the first group are lesions such as those in Dr. Waddington's patient. Histologically they are almost spherical nodules of an even mixture of cells of the reticuloendothelial series, ranging from large reticulum cells down to lymphocytes and including many eosinophils and small giant cells. The blood vessels in the infiltrated area show gross enlargement of their endothelial nuclei and give the impression that they may be the origin of the free reticulum cells and the small giant cells.

We have examined material from 5 such cases so far and in each one the conspicuous features are the even mixture of the cells and the lack of organization into germinal follicles. These 5 cases in addition to having a similar histology have closely resembled each other clinically. The

lesions have in each case been multiple (ranging from 4 or 5 to hundreds), small (up to 1 m. diameter) confined to exposed surfaces and all have been sensitive to light—swelling and itching on exposure to strong sun. So far none of these cases has shown involvement of tissues other than exposed skin. Two cases have been followed for twenty and twelve years respectively but longer follow-up on more cases will be required before this state can be confidently labelled benign. From its behaviour it would seem likely that it is to some extent the result of exposure to light.

The second type of lesion is that which we call follicular lymphoma. The histology of these consists of multiple discrete and confluent, fairly sharply margined accumulations of lymphocytes in the centre of which are to be found germinal centres of large reticulum cells. The structure of such lesions appears to be identical with the lymphoid tissue which develops in the dermis sometimes in lupus erythematosus, primary atrophy of the vulva and other chronic inflammatory states. In follicular lymphoma, however, the presence of the lymphoid tissue is unaccompanied by other changes in the skin.

Clinically the lesions of follicular lymphoma differ from those of the first group in growing to a larger size (up to a inch or more in diameter), not in confining themselves to exposed sites and, when they do affect such sites, in not being light-sensitive. In addition, the skin deposits of follicular lymphoma are frequently accompanied by glandular ones and both appear able by a process of gradual transition to become one of the malignant lymphomas, reticulum-cell sarcoma, Hodgkin's disease and so on.

The PRESIDENT asked whether there was any known way of dealing with the cases.

Dr. H. R. Vickers: Dr. Rupert Hallam and I described 2 cases in 1939 (*Brit. J. Derm.*, 51, 251) and both these cases responded well to superficial x-ray therapy, 3 exposures of 133 r at fortnightly intervals.

Dr. M. SYDNEY THOMSON: It might be helpful to undertake further study of the foetal skin in this connection, for we must not forget the embryological functions of that tissue. It may be possible to distinguish then between these two groups.

Two Cases of Multiple Naevoid Basal Cell Epitheliomata ? Porokeratosis of Mantoux.—Dr. C. D. CALNAN (for Dr. F. R. BETTLEY).

I. W. B—, female, aged 33.

History (2–3 years).—Insidious onset of small nodules on the face, especially the temple areas. No symptoms. None have resolved spontaneously. No previous treatment. The condition of the palms has been present since childhood. No history of arsenical medication elicited. No changes noted during recent pregnancy.

Family history.—No similar lesions known in relatives who have not been examined.

Examination.—*Face*: There are 30 or more pearly nodules distributed over the face. Many are aggregated over the lateral aspect of the forehead. On the left side there is a telangiectatic atrophic patch of irregular shape, about 1 cm. × 2 cm. surrounded by these nodules. The latter vary in size from 1 mm. to 5 mm. in diameter. Most are flesh coloured or translucent. A few are superficially ulcerated.

In addition there are milia and a few cellular naevi.

Palms: Over the palms and palmar surfaces of the fingers are pinhead-sized hyperkeratoses from many of which the central core appears to have fallen out, leaving a small pit with borders slightly elevated above the rest of the skin; no surrounding erythema (Fig. 1). The intervening skin is quite normal.

There is a similar appearance on the soles, where the picture is modified by the normal thicker stratum corneum.

Histology.—A lesion from the left side of the forehead shows a basal-cell epithelioma without signs of differentiation into appendages. There is some myxomatous degeneration.

II. E. D—, female, aged 44.

History.—1935: Onset of small nodules on the face.

1939: The largest lesion below right eye was treated with radium, and also with CO₂ snow, and diathermy.

1948: Many new lesions appeared. One of these was removed for section (Section 1).

1949: Some fresh nodules erupted. One on the right temple showed signs of breaking down and was excised.

1950 : Another lesion was examined histologically (Section 2).

1952 : Few new nodules. A further biopsy (Section 3).

The condition of the palms has been present since childhood.

Past history.—Operation on left temporo-mandibular joint.

Family history.—She states that her mother had one lesion similar to her own.

Examination.—*Face* : There are 16 to 20 pearly nodules scattered asymmetrically over the face and right postero-lateral side of the neck. They vary in size from 1 mm. to 5 mm. in diameter. Below the right eye is the scar of the first treated lesion.

A few show signs of ulceration.

She also has a few cellular naevi and milia.

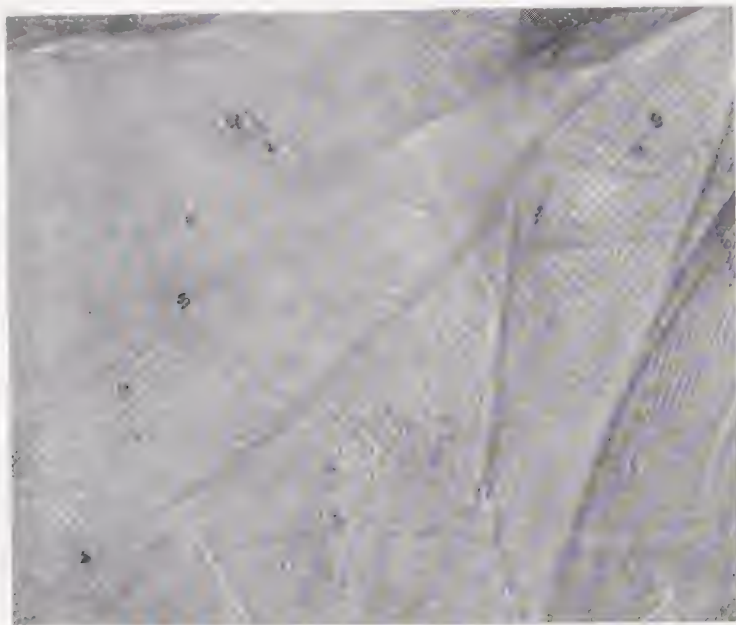


FIG. 1.

Hands : The palms and palmar surfaces of some fingers show pinhead-sized keratotic lesions and small pits. They are symmetrical. Each is a small localized area of hyperkeratosis, without any erythema, and the intervening skin is quite normal. There is a similar condition on the soles.

Histology.—*Section 1* : There are several branching strands of typical basal-cell epithelioma exhibiting cysts and deriving their origin from the atrophic epidermis. There is mild lymphocytic and fibroblastic reaction to the tumour.

Section 2 : The histology is that of an ulcerating basal-cell epithelioma with myxomatous degeneration. There is a heavy infiltration of round cells around the tumour. Under polariscope examination there is a hair shaft lying within the tissue and enveloped by the basal-cell tumour, probably indicating that part of the tumour derives its origin from the follicle, leading to its destruction.

Section 3 : The epidermis is thinned and the cutis shows long islands and strands of basal-cell epithelioma lying within a homogenized collagen. The tumour derives its origin both from the follicles and the epidermis. Three calcified foci can also be detected. The lymphocytic infiltration is heavy and the histology resembles that of a morphoeic type of basal-cell epithelioma.

Comment.—Instances of more than one rodent ulcer, up to perhaps six in number, are not rare, but these two patients' lesions merit separate description.

Dr. Adamson (1908) was probably one of the first to draw attention to these cases of multiple naevoid basal-cell epitheliomata and distinguish them from epithelioma adenoides cysticum of Brooke. He described two cases of his own and noted three similar ones in the literature which were labelled Brooke's disease—one in Stelwagon's book and one each by White (1894) and Jarisch (1894). Sequeira (1919) also saw a case which is probably the one illustrated in his text book. Later Sir Norman Paul (1933) described three cases, one of whom, it may be noted, had a superficial basal-cell epithelioma on the back. Similar patients have recently been shown here by Scott (1952) and Waddington (1952).

All these cases seem to conform to one type, but other varieties of multiple epithelioma have been described: such as zoniform, both of the superficial (Witton and Lazar, 1952) and ordinary basal-cell type (Adamson, 1917); the patients shown by Yorke (1950), Barber (1924), and Glen (1945) are different. A remarkable case was described by Pautrier (1947) of numerous basal-cell epitheliomas on the face, scalp and trunk in a girl of 19 who had had them since the age of 4.

The condition of the palms appears to be the same in both patients. I have made a tentative diagnosis of Porokeratosis of Mantoux because it resembles a patient seen in Professor Gans' clinic in Frankfurt early this year.

The subject is discussed in Jadassohn's *Handbuch* by Moncorps (1931) and in the *Nouvelle Pratique Dermatologique* by Louis Chatellier (1936). The published cases vary both in their morphology and natural history. Few cases have been recorded with the very small individual lesions as in my patients.

The dermatosis is now regarded as naevoid, and not necessarily a keratosis of the sweat pores.

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DR. HUGH GORDON: These multiple basal-cell epitheliomata are not in themselves particularly uncommon. For instance, at the Royal Cancer Hospital we have two members of one family attending, of whom one has had ten lesions treated, and the other over fifty. They were all very superficial: rather more so than the case shown. The association in this case with the hand lesions is interesting.

THE PRESIDENT: Sir Norman Paul underlined the association of these very numerous basal-cell epitheliomas with a variety of facial naevi.

Erythema Chronicum Migrans (Lipschütz).—Dr. S. C. GOLD.

K. W.—male, aged 26, was first seen in May 1951 with a lesion on the inner side of the right ankle that had been present for two months.

History.—In September 1950 he was bitten by an insect on the lower shin and afterwards a small brown mark persisted for six months; later it started to swell like a blind boil and discharged. The nodule gradually increased in size and the clinical diagnoses considered were sarcoid and nodular vasculitis. Histological findings at that time were consistent with the latter.

Investigations.—Wassermann and Kahn reactions: negative. E.S.R.: 34 mm. in one hour (Wintrobe). Total W.B.C.: 6000 per cu. mm. Eosinophils: 9%.

Progress.—Within a few months the lesion had spread centrifugally, the centre being yellow and pigmented and the edge a raised red band with a serpiginous contour; the surface was slightly scaly. The lesion would have periods of activity when the edge would swell and spread; these would alternate with periods of quiescence when the edge would flatten. On two occasions a week's course of Sulphatriad appeared to suppress the activity. By August 1952 the ringed erythema was now three times its original size. The band-like margin would be as much as 2 cm. wide and of a dusky red colour. The clearing central zone showed a few scattered scars from previous ulceration but otherwise there was no atrophy; the centre was patchily pigmented.

POSTSCRIPT.—A course of systemic penicillin, 600,000 units daily for ten days, has not influenced the condition which is active once again.

Dr. R. D. SWEET: I had hoped to bring up another patient with this condition, a farmer whom I saw early in the spring. When cleaning out his chicken-house he was bitten by numerous fleas. He developed about 30 or 40 ringed lesions which were spread over his trunk and had a pale pink border. Many of these rings fused to produce bizarre patterns rather as if a child had been doodling. After about 6 months they all gradually faded and there was nothing to show where they had been.

Dr. H. HABER: In the corium is an acute inflammation with extravasation surrounding small blood vessels which show thrombosis and necrosis of their walls. The histological picture reminds one of an Arthus' phenomenon.

Lichenoid Gold Eruption.—Dr. R. H. MEARA (for Dr. G. B. DOWLING).

W. E. W—, male, aged 51.

History.—For the last three years this patient has suffered from rheumatoid arthritis.

Eight months ago a course of gold injections was started, one injection being given weekly, for five months, when an irritable rash appeared on both forearms. The gold injections were stopped, but the eruption became more widespread until, after three weeks, all parts of the body were involved. At this time he was given a course of B.A.L. (16 ml. being given over a period of four days). Apart from slight subjective improvement lasting a few days this produced no change. The eruption remained very irritable until about three weeks ago, when it began to improve.

Examination.—The lesions are present on all parts of the body. On the face there are many hyperkeratotic faintly purplish papules closely set on the forehead; the trunk and limbs show oval and discoid lesions up to 1.5 cm. in diameter, some deeply pigmented, others still showing a faint violaceous hue. These lesions are made up of lichenoid papules and many of them show an irregular, flat, depressed area in their centres. The palms show discrete, purplish, slightly hyperkeratotic papules, while on the ankles and feet the lesions are more hyperkeratotic and purpler in colour. The buccal mucosa on the left side shows a few white streaks which represent the relics of more obvious lesions which have resolved. There is diffuse scaling of the scalp. No abnormalities were found in other systems except for some swelling of the proximal interphalangeal joints of the fingers of both hands.

Investigations.—Urine: normal. White cell count: Total 12,600. Normal differential. W.R. and Kahn: Negative.

Histology (Dr. H. Haber).—The epidermis shows loose hyperkeratosis, acanthosis and, in some places, a saw-tooth-like appearance of the epidermo-dermal junction.

The lower part of the epidermis shows oedema and immigration of round cells. The papillary body exhibits oedema and perivascular round cell infiltration mixed with chromatophores heavily laden with melanin. A few hyaline blocks of collagen and hyaline degenerated epidermal cells can also be detected. The infiltrate runs also along the blood vessels of the stratum reticulare.

The histology resembles, in some places, that of lichen planus.

Comment.—This patient illustrates the close resemblance that may exist between this type of eruption and lichen planus.

So close is this resemblance, both clinical and histological, that it may be more correct to consider this a case of lichen planus provoked by gold.

Dr. J. E. M. WIGLEY: I do not always find it easy to differentiate between the "lichenoid gold eruption" and lichen planus. The present case seems to me very typical of lichen planus and I think the history of gold treatment may well be a coincidence.

Dr. J. OVERTON: Has anyone used Cortisone for treatment of this condition which sometimes can be very disfiguring, particularly in women? I tried a case on Cortisone by injection—300 mg., 200 mg., and then 100 mg. a day for a month with no apparent response. Incidentally, a previous course of B.A.L. had produced no improvement.

Dr. B. SCHWARTZ: In a case I saw part of the biopsy material cut in the usual fashion showed the pathology of lichen planus; the other part was subjected to spectrographic examination and showed an appreciable amount of gold present. The normal skin did not show gold in the same biopsy. That might be a means of differentiation between true lichen planus and one produced by gold.

The PRESIDENT: The remarkable point about these gold lichenoid eruptions is that they have a certain rather characteristic appearance—a dusky colour and also an associated lichen spinulosus which is a very striking feature of this case and has been so in others of the same origin.

Ectodermal Dysplasia with Universal Pili Torti: Retinitis Pigmentosa.

Dr. D. S. WILKINSON.

Mr. E. C—, aged 56 years.

When this patient originally came to the clinic because of an eruption of warts on the forearm, it was noticed that he showed several features of congenital ectodermal dysplasia.

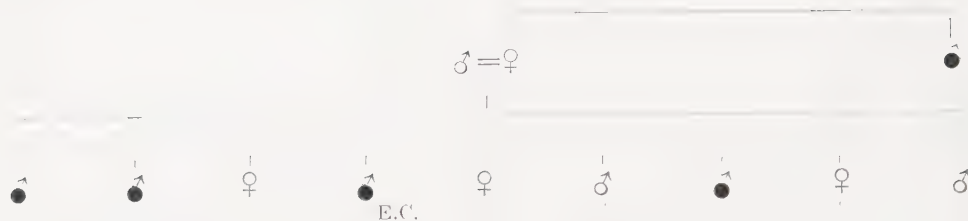
Since childhood his hair has grown poorly and has broken easily. During adolescence, the outer half of the eyebrows and the eyelashes gradually disappeared. His teeth have always been poor and were removed early in life. His body hair did not develop naturally, and has never grown long. He states that he does not sweat normally, even on exertion, and having many brothers and sisters, has been able to compare himself with them in this respect. He is not unduly oppressed, however, by hot weather. His axillary sweating is normal.

He suffered from night-blindness and was referred to Mr. Victor Purvis, consultant ophthalmologist, who diagnosed retinitis pigmentosa.

On examination—He is well built and well proportioned. There is no infantilism. There is perhaps some parietal bossing of the skull and, over this region particularly, the hair is thin. All the scalp hair is coarse and breaks off at a length of three or four inches. The body hair is very sparse and though the follicles are present, many of them carry a very small wiry, curled hair or only a keratin plug. Hairs from the body, pubis and the scalp all show twisting through 180°. The pubic hair resembles the scalp hair. The teeth are false, the nails normal. Intelligence is good. He shows retinitis pigmentosa of the scattered type in both eyes.

Family history (retinitis pigmentosa).—As far as the patient and one brother know it, the family history is given below. Further details are being collected. He is the only one of the siblings to show this peculiarity of the hair. All the adults of the family have artificial teeth. Obviously, the presence of retinitis pigmentosa cannot yet be confirmed in the children. Three of the brothers have suffered from "eczema".

Comment.—The condition of pili torti is usually seen limited to the scalp, eyebrows and eyelashes and not associated with other anomalies. In this patient, a multiple



genetic disturbance seems to exist with hypotrichosis, poor sweat function and family history of bad teeth. The case probably corresponds with Gentili's group of congenital hypotrichosis, in which functional or qualitative changes in the hair follicles lead to alteration in the hair shaft and in which sweat or sebaceous glands may also be affected. It is inherited as a recessive.

The retinitis pigmentosa is probably coincidental. It may be associated with cataract, deafness, mental defect and so on, but it is doubtful whether there is ever any true association with abnormalities of the skin. The cause is disputed, being regarded either as an abiotrophy of retinal cells or as a vascular defect. Inheritance is variable.

POSTSCRIPT.—Since this case was shown, Dr. Martin Beare has recorded rather similar cases and he has drawn my attention to the similarity of this case to those described by Ullmo and his own cases.

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Lichen Sclerosus et Atrophicus of Trunk and Penis (? Early Balanitis Xerotica Obliterans).—Dr. BRIAN RUSSELL.

C. K—, male, aged 26 years.

History.—In October 1951 he noticed a white patch on the chest. It is now 3.5 cm. in diameter, irregularly circular, an atrophic white plaque showing follicular plugging. There are also two white guttate lesions with follicular plugging on the right shoulder. On the penis there is perimeatal atrophy without stenosis of the orifice. Smaller atrophic patches are visible elsewhere on the glans penis. When first seen, the patient was unaware of the presence of these lesions and he has had no difficulty with micturition.

Histology.—Biopsy from the sternal lesion shows atrophy of the epidermis with scanty horny plugs, small subepidermal foci of oedema, and a patchy infiltration of lymphocytes and histiocytes in the dermis.

Montgomery and Hill (1940 *Arch. Derm. Syph., Chicago*, **42**, 755), described 38 patients with lichen sclerosus et atrophicus, 8 of whom were males. Two of the men had penile involvement.

Freeman and Laymon, (1940 *Arch. Derm. Syph., Chicago*, **49**, 57), described 18 cases of balanitis xerotica obliterans and suggested that this condition might be lichen sclerosus et atrophicus confined to the penis; in their patients search had not been made for lesions of lichen sclerosus et atrophicus elsewhere; but in a subsequent paper these authors noted lichen sclerosus et atrophicus in 5 of

6 further patients with balanitis xerotica obliterans, and concluded that the two conditions are the same disease, showing on the penis either as isolated papules of lichen sclerosus et atrophicus on the shaft or as a constricting preputial band with plaques on the glans and with urethral stenosis.

Dr. BRIAN RUSSELL: The constricting preputial band is an important feature of balanitis xerotica obliterans as it affects the uncircumcized penis. Retention of smegma by this band may be the cause of the subpreputial infection.

The following cases also were shown :

Case for Diagnosis. ? Malignant Granuloma.—Dr. D. E. OAKLEY.

Disseminated Granuloma Annulare, Showing Necrobiosis Maculosa (Miescher).—Dr. I. S. HODGSON-JONES.

Squamous-cell Epithelioma.—Dr. R. H. SEVILLE and Dr. D. S. ANDERSON.

Pachyonychia.—Dr. B. SCHWARTZ.

CURRENT LITERATURE

EXPERIMENTAL SIMULATION OF THE L.E. PHENOMENON. H. SILVER and A. KUNA. (1952) *J. invest. Derm.*, 19, 281.

It has been supposed that the L.E. cell is linked in some way with abnormality of the plasma protein. The authors believe that in the course of tissue damage in L.E. nuclear protein is liberated and at the same time certain polysaccharides, e.g., desoxyribonucleic acid. The polysaccharide is supposed to become adsorbed on to the surface of the nucleoprotein and attract leucocytes just as jam on a piece of bread and butter attracts wasps. If a blood film is fixed, soaked for 10 mins in a 5% solution of glycogen, washed, dried, and then a suspension of leucocytes in plasma is placed in contact with it, the leucocytes will form rosettes around the leucocytes in the film. Leucocytes will also swarm round a grain of starch. They merely clump in a solution of desoxyribonucleic acid: but they also clump round the amorphous material that occurs in a suspension to which trypsin has been added.

J. H. T. D.

THE KIDNEY OF SCLERODERMA. H. C. MOORE and H. L. SHEEHAN. (1952) *Lancet*, 1, 68.

In generalized scleroderma arterial lesions may be found, not only in the skin and subcutaneous tissue but also in viscera such as intestines, lung and oesophagus. The present report is about the findings in the kidney in three fatal cases of the disease. The specific type of renal lesion which caused death is described. The larger intralobular arteries were dilated and had developed a peculiar mucoid intimal thickening; and the smaller arteries were subsequently affected by fibrinoid necrosis. The resulting ischaemic necrosis of the cortex led to renal insufficiency and eventual death in about two to four weeks after the onset of the renal damage.

R. H.

A CASE OF SCLERODERMA. J. N. BRIGGS and R. S. ILLINGWORTH. (1952) *Lancet*, 1, 346.

This paper records the complete failure of three recommended drugs in a severe degree of scleroderma in a girl aged 13 who was treated with sodium *p*-aminobenzoate (PABA), adrenocortico-trophic hormone (ACTH), and 4-3-hydroxy-2-phenyl-cinchoninic acid (HPC). There was no response to treatment, slow deterioration occurring throughout.

R. H.

XERODERMA PIGMENTOSUM. D. W. SMITHERS and J. H. WOOD. (1952) *Lancet*, 1, 945.

Protection of the skin from sunlight by means of local applications in a patient suffering from xeroderma pigmentosum. It was found that the substance with the best covering power was titanium dioxide, and a vanishing cream base containing this was eventually elaborated. It was found to be clinically effective and cosmetically acceptable. The cream is available from Elizabeth Arden Ltd.

R. H.

DISSEMINATED LUPUS ERYTHEMATOSUS COMPLICATED BY MILIARY TUBERCULOSIS DURING CORTISONE THERAPY. J. N. HARRIS-JONES and N. K. PEIN. (1952) *Lancet*, 2, 115.

The increasing use of ACTH (adrenocortico-trophic hormone) and cortisone has attracted attention to the potential dangers of these hormones in the presence of known or unsuspected

tuberculosis. In the case reported a woman aged 36 who was given cortisone for disseminated lupus erythematosus developed miliary tuberculosis with positive sputum and urine, despite the fact that she had previously been under observation for four years without evidence of tuberculosis being found at any time. It seemed likely that the disease spread from a latent focus directly activated by cortisone. She fortunately responded satisfactorily to streptomycin and para-aminosalicylic acid.

R. H.

ANOGENITAL PRURITUS. R. D. SWEET. (1952) *Lancet*, 2, 258.

In this very interesting paper the origins of anogenital pruritus are discussed and reasons suggested for its persistence. It is thought usually to be a variant of lichen simplex which is perpetuated by scratching after the precipitating cause has long ceased to operate. The relative value of x-rays and psychiatry is discussed together with indications for their use.

R. H.

SUPERFICIAL STAPHYLOCOCCAL INFECTION. VALENTINE and HALL-SMITH. (1952) *Lancet*, 2, 351.

In most cases of persistent furunculosis and sycosis barbae the anterior nares contain the same strain of staphylococci as that found in the lesions. Occasionally, instead of the nose, the eye or some other region is the "reservoir" from which the infection continues to be discharged. The infection also persists in the neighbourhood of the lesion until it is completely healed. A course of treatment is described based on a simple explanation to the patient that infection is spread to other parts of the body from the lesions or nose by fingers or handkerchief. All lesions were treated until healed, and terramycin ointment was used on the "reservoir" twice daily for one month. The clinical results were good. Sensitization of the skin to terramycin appeared to be uncommon.

R. H.

THE CAUSE AND TREATMENT OF LEG ULCERS. S. T. ANNING. (1952) *Lancet*, 2, 789.

The development of the knowledge of the aetiology of leg ulcers is reviewed historically in this comprehensive article. The importance of an increase in venous and capillary pressure in the lower part of the leg is emphasized, the essential defect being shown to lie in the valves of the deep veins of the lower limb. In 715 patients the cause of such trouble was venous thrombosis in 80% and varicosity of deep veins in 7%. Ulcers due to hypertension are described and the problem of arterial and arteriolar disease in relation to leg ulcers is discussed. In addition to methods of prevention, treatment by rest, elastic support, massage and surgery are considered, and suggestions made for after-care.

R. H.

CONGENITAL VACCINIA AND VACCINIA GRAVIDARUM. PATRICK McARTHUR. (1952) *Lancet*, 2, 1104.

A case of congenital vaccinia is recorded following vaccination of a pregnant woman at the end of the third or beginning of the fourth month of pregnancy. The mother developed a severe primary reaction and three months later was spontaneously delivered of a feeble hydropic premature infant covered with a very severe generalized vaccinia. The child died 18 hours after birth. It is noted that congenital vaccinia has only once before been described (Lynch, 1932). An analysis of the results of 203 pregnancies in which the women were vaccinated immediately before and during pregnancy showed a highly significant increase in mortality among the fetuses of women vaccinated during the first three months of pregnancy.

R. H.

THE IMPORTANCE OF CYTOLOGICAL INVESTIGATION IN THE DIFFERENTIAL DIAGNOSIS OF BULLOUS SKIN DISEASES. A. KEMPER. (1953) *Derm. Wschr.*, 127, 97.

Smears as thin as possible are dried in the air and stained with May-Grünwald-Giemsa solution like a blood film. Among the bullous eruptions investigated that showed a characteristic picture helpful in differential diagnosis were pemphigus vulgaris (7), herpes zoster (3) and varicella (2); also a cantharides blister in acute lupus erythematosus. Ten photomicrographs clearly illustrate the text. Normal controls were investigated by means of a cantharides blister and showed neutrophil leucocytes, occasional lymphocytes and a relatively large proportion of histiocytes; sometimes erythrocytes following vigorous scrubbing, and traces of protoplasmic bridges giving a palisade appearance to the epithelial cells. This was more or less the picture obtained from

dermatitis herpetiformis (10), eczema mycoticum bullosum, erythema multiforme, bullous pyoderma, bullous dermatitis, epidermolysis bullosa, chronic erythematodes with exacerbation, and herpes gestationis, apart from an occasional eosinophil. In pemphigus the filamentous element of the epithelial cells was lost and the nucleus was round or oval, sometimes staining deeply, and the cells, though isolated one from another, had a grouped placard arrangement. They were not altered by treatment. A similar appearance was obtained from mucous membrane lesions, and as the finding was constant in all the pemphigus patients examined it allowed of differential diagnosis from dermatitis herpetiformis, often difficult clinically.

Smears from herpes zoster (3) and varicella (2) showed balloon cells and giant cells with 6-8 nuclei or a single very large deeply staining nucleus. Fresh blisters are necessary for the finding. A cantharides blister in the immediate neighbourhood did not give this picture; nor did scrapings from vaccinia inoculata (1). Herpes simplex should show a similar characteristic appearance.

A cantharides blister in acute lupus erythematosus showed typical L.E. cells or rosette forms (Wright's blue solution) in all 5 patients examined but were absent in 2 patients with an acute exacerbation of chronic erythematodes, and they are not found in dermatomyositis, generalized scleroderma or periarteritis nodosa.

M. S. S.

EPIDERMODYPLASIA VERRUCIFORMIS (LEWANDOWSKY—LUTZ) AND VITAMIN A.

E. IANDES. (1952) *Derm. Wschr.*, **126**, 1130.

Vitamin A in full doses was found to make warty lesions virtually disappear in a woman aged 44 (consanguinity of parents) with the above disease. Several spino-cellular carcinomata of the face and back of hands (areas exposed to light) were removed with contact x-ray therapy. The usefulness of vitamin A in hyperkeratosis due to vitamin deficiency or in congenital dyskeratoses (ichthyosis, Darier's disease, and pityriasis rubra pilaris) prompted the author to use it here. The histological appearances were reminiscent at times of Bowen's disease and at times of Darier's; changes were greatest in the upper layers of the stratum spinosum with deformity of cell nuclei and intercellular and intracellular oedema. Corps ronds were present, and there was much proliferation of the horny layer, atypical cornification but no inclusion bodies. The cell degeneration strongly suggested a precancerous state and the histology of a brow lesion an early spino-cellular carcinoma.

Vitamin A was given in doses of 50,000 units orally *t.i.d.* (and for 12 days 300,000 units were given intramuscularly daily). The treatment was continued for six months and she received altogether 37,100,000 units vitamin A. After a rest for six months lesions tended to recur but responded again to treatment. No fresh lesions appeared after the institution of treatment with vitamin A. It is suggested that in this condition there is a congenital factor, and defective absorption of vitamin A or derangement in the conversion of the provitamin.

M. S. S.

ACETARSOL PESSARY DERMATITIS. J. O. DOYLE. (1952) *Brit. J. vener. Dis.*, **28**, 210.

A married woman aged 31 of somewhat neurotic temperament became sensitized to a pentavalent arsenical following absorption through the vaginal mucosa. The possible aetiological factors are discussed, and the dramatic response to local therapy and B.A.L. is noted. Patients under treatment with acetarsol pessaries should be carefully observed at frequent intervals, and the use of the pessaries should be immediately discontinued if any local erythema of the external genitalia or thighs appear.

W. G. A.

DERMATOLOGY AMONG THE SPECIALTIES: A PLAN TO ACHIEVE ITS DESIRED STATUS.

S. M. PECK. (1952) *J. invest. Derm.*, **19**, 259.

The President in his address to the 13th annual meeting of the Society for Investigative Dermatology deploras "the continuous downward spiral as far as attracting good men to our specialty is concerned . . . never were dermatologists better trained than they are to-day, never has the status of the specialty fallen so low." The remedy is to be research in acne and psoriasis. Research to-day is impossible without lots of money. Although in most instances one still has to wait for the good idea to germinate in the mind of some brilliant and often independent-minded individual, it is going to cost vast sums to carry the idea out, all the cheap things having been thought of already. Let therefore the various dermatological societies get together to form a publicity organization for the purpose of collecting the money needed. The existence of a fund is all you need to attract the best brains.

J. H. T. D.

EXPERIMENTAL ANIMAL INVESTIGATIONS ON BEHAVIOUR OF TUBERCLE BACILLI IN LUPUS VULGARIS AFTER THIOSEMICARBAZONE AND CALCIFEROL. G. VELTMAN. (1951) *Arch. Derm. Syph., Berl.*, **193**, 305.

Even though clinically healing or healed, lupus nodules contained virulent tubercle bacilli after thiosemicarbazone or high dosage calciferol therapy. Excised tissue was inoculated into guinea-pigs and tubercle bacilli were isolated from 15 of 23 patients. M. F.

PENICILLIN HYPERSENSITIVITY. W. LINDEMAYR. (1951) *Arch. Derm. Syph., Berl.*, **193**, 325.

A useful summary leading to the following advice: use penicillin locally only where there is a strict indication and for no more than 3-5 days. Especial care is necessary in patients who have reacted previously, have fungus infections, or are allergic. Intracutaneous testing is relatively the best way of demonstrating hypersensitivity. Beware of accidental intravenous injection. Use antihistamines prophylactically. M. F.

THE FATTY MANTLE OF THE SKIN AND ITS SIGNIFICANCE IN WETTING THE SKIN SURFACE. W. SCHNEIDER and H. SCHULEIT. (1951) *Arch. Derm. Syph., Berl.*, **193**, 434.

The fatty mantle of the skin is not a water repellent, but, owing to its various components, serves as a regulator of the water content of the skin. Apart from the main fatty constituents, there are alcohol- and water-soluble substances in the mantle, the chemical composition of which is not yet determined, which serve to wet the hydrophobe keratin of the skin surface. M. F.

ANTIBIOTICS IN ACTINIC DERMATITIS. J. DAŃNOW. (1951) *Dermatologica*, **102**, 307.

In two cases of severe actinic dermatitis which had lasted for years the stools contained haemolytic cocciform bacilli and a high content of porphyrins. Treatment with Gantrisan, 3.0 g. daily for a fortnight, suppressed the bacilli, reduced the porphyrin content of the stools, and cured the patients, who remained well throughout the summer. J. F. S.

CORTISONE AND EXPERIMENTAL CONTACT DERMATITIS IN GUINEA-PIGS. J. R. FREY and A. STUDER. (1951) *Dermatologica*, **103**, 65.

Using a quantitative technique, the authors found that cortisone exerted no obvious influence on the development of sensitization towards dinitrochlorbenzol, on its degree, or on its histological picture. J. F. S.

STUDIES ON PIGMENT-FORMATION IN THE SKIN. H. R. LIEBETRAU. (1951) *Dermatologica*, **103**, 75.

These studies were undertaken primarily to confirm or refute Zeller's theory that a dark pigment is produced when histaminase acts on histamine. Confirmation was entirely lacking. Liebetrau found the copper content of the blood normal, or at any rate not decreased, in vitiligo. In Riehl's melanosis and in chloasma, apart from pregnancy, values were always above normal, so that copper might conceivably be a factor in the aetiology of the latter two dermatoses. J. F. S.

CYTOLOGICAL OBSERVATIONS IN BULLOUS DERMATOSES BY PHASE-CONTRAST MICROSCOPY. E. U. MIAN. (1951) *Dermatologica*, **103**, 89.

Mian studied with the phase-contrast microscope suspensions of cells, taken with the utmost gentleness from blisters in pemphigus, dermatitis herpetiformis, impetigo and cantharides blisters. "Potoecytosis" and degenerative changes could be studied from their beginnings, and were morphologically similar in all these conditions, but the tempo was very different. In pemphigus these changes had usually started within three minutes, but in cantharides blisters only after thirty minutes. He also studied the effects of different suspension solutions on these changes, but although he observed very striking changes, he was unable to work out any constant differences between cells from pemphigus and those from normal epidermis. J. F. S.

THE INFECTIVITY OF SHOES AND STOCKINGS IN TINEA PEDIS. E. FISCHER. (1951) *Dermatologica*, **103**, 97.

320 cultures from fibres taken from socks, stockings and parings from inside shoes, from 142 cases of tinea pedis, yielded only two growths, both of *E. Kaufmann-Wolf*. Artificial infections

of wool, cotton, rayon, silk and nylon proved that *E. Kaufmann-Wolf* and *Tr. gypseum* do not penetrate the fibres, and that these materials can be sterilised effectively by soaking for 24 hours in 1 in 5000 Merfen, 2% Desogan or 1 in 1000 Bradisol. J. F. S.

PYODERMIA CHRONICA VEGETANS OF AZÚA. J. GAY PRIETO and M. A. CASCOS. (1951) *Dermatologica*, 103, 135.

The authors describe 5 cases, representative of a much larger number seen in their practice, of the condition first described by Azúa in 1894 under the title of "epitelioma excrecente pseudo-inflamatorio," and in later publications as "pseudo-epitelioma cutaneo." Peyri in 1926 summarized observations to date under the name of "vegetating pyodermias." Gay Prieto and Cascos were led to review their material and write this paper by recent publications under the heading of "papillomatosis cutis carcinoides," which they believe to be identical with Azúa's dermatosis, and they go a long way towards establishing this. The writer of this abstract published in 1929 the first British account of the condition, and in ignorance of the Spanish work ascribed priority to E. Hoffmann. He welcomes this belated opportunity to acknowledge the long priority of Azúa. J. F. S.

DYSKERATOSIS CONGENITA (COLE). L. H. JANSEN. (1951) *Dermatologica*, 103, 167.

Cole in 1926 demonstrated to the Cleveland Dermatological Society a "new" syndrome of ectodermal anomalies—pigmentation; atrophy of the skin of the backs of the hands and fingers; leukoplakia-like changes in the mouth; palmar and plantar hyperidrosis and obliteration of the puncta lachrymalia. Two pairs of brothers similarly affected have since been reported in America, and Jansen now records a sixth case, the first from Europe. His patient has also haemorrhagic blisters on his fingers, suggesting an affinity with epidermolysis bullosa. He dislikes the term "dyskeratosis," which is usually employed to denote the peculiar epidermal change so named by Darier, and he suggests the beautiful and concise alternative title of "pigmentatio parvoreticularis cum leukoplakia et dystrophia unguium." J. F. S.

THE HISTOPATHOLOGY OF THE FREI REACTION. M. DEPAOLI. (1951) *Dermatologica*, 103, 158.

In 5 cases of lymphogranuloma venereum the site of Frei's intradermal reaction, which could then barely be felt, was excised two to nine months after the injection. In three there were still pronounced changes, which could scarcely be residual and must be considered to be due to local settling of the virus which was presumably circulating in the blood at the time of the test. J. F. S.

THE PROTEINS IN BLOOD AND BLISTER-FLUID IN PEMPHIGUS AND OTHER BULLOUS DISEASES. C. H. BECK. (1951) *Dermatologica*, 103, 365.

Hypoproteinaemia and dysproteinaemia are regularly found in pemphigus vulgaris; dysproteinaemia alone in other extensive bullous diseases. The blister-fluid in p. vulgaris differs from others in that it shows a lower albumin-globulin ratio than that in the blood of the same patient, while in other bullous dermatoses the proteins in the blister-fluid reflect accurately those in the blood. This is held to support the view that the blister in p. vulgaris owes its origin to epithelial degeneration, and not to vascular disturbance. J. F. S.

THE ACTION OF CORTISONE ON THE RESTING AND STIMULATED SKIN OF RATS. A. STUDER and J. R. FREY. (1952) *Dermatologica*, 104, 1.

Injections of cortisone inhibited mitotic activity in resting rat epidermis, and led to thinning of both epidermis and corium. High doses of vitamin A or of testosterone propionate stimulated the skin to great activity, but this effect was largely prevented by cortisone. The authors discuss the bearing of these findings on the atrophy of the skin seen in Cushing's syndrome, and on the therapeutic use of cortisone in certain skin diseases. J. F. S.

THE CLINICAL OBSERVATIONS OF JONATHAN HUTCHINSON. VICTOR A. MCKUSICK. (1952) *Amer. J. Syph.*, 36, 101.

A review of Jonathan Hutchinson's wide clinical acumen and a recording of his recognition of the significance of many dermatological conditions. D. E.

THE INCIDENCE OF POSITIVE SEROLOGIC TESTS FOR SYPHILIS IN THE COLLAGEN DISEASES. HENRY E. ZELLMANN. (1952) *Amer. J. Syph.*, **36**, 163.

A retrospective study of positive serological reactions detected in patients receiving treatment for various collagen diseases. Only 20 out of 82 serological positive cases were considered syphilitic. In the remainder presumably biological false positive reactions varied from time to time, and were more common in cases of lupus erythematosus and periarteritis nodosa than in patients suffering from dermatomyositis, scleroderma or rheumatoid arthritis. The author observes that the significance of these tests is of little value as the presumably false positive reactions were not then subjected to modern technique.

D. E.

TREATMENT OF SYPHILIS WITH AUREOMYCIN AND CHLOROMYCETIN. S. R. TAGGART, M. J. ROMANSKY and G. S. LANDMAN. (1952) *Amer. J. Syph.*, **36**, 174.

Twelve months' observation of patients in various stages of early syphilis indicates a possible therapeutic value of oral aureomycin or chloromycetin in a dose of 60 mg. per kilo per day for 8 days.

D. E.

A FIVE-YEAR STUDY OF ANTIBIOTICS IN THE TREATMENT OF GRANULOMA INGUINALE.

ROBERT B. GREENBLATT, WM. E. BARFIELD, ROBERT B. DIENST, ROBERT M. WEST and MILTON ZISES. (1952) *Amer. J. Syph.*, **36**, 186.

295 cases were treated. Although 8 failures occurred in 142 patients treated with streptomycin, 4 g. daily for 10 days, no failures were recorded in 71 patients treated with aureomycin, and 36 treated with terramycin, 2 g. daily for 10-20 days in each case. Of 41 cases treated with chloromycetin, 1 was resistant.

D. E.

SPECIAL DIAGNOSTIC AND THERAPEUTIC PROBLEMS IN SYPHILIS. CHARLES R. REIN and GEORGE H. KOSTANT. (1952) *Amer. J. Syph.*, **36**, 301.

A discussion on the problems of diagnosis and management of patients with positive blood reactions. The comparative safety of penicillin therapy is considered a great temptation to administer treatment without careful exclusion of false positive reactors with repeated quantitative tests and special laboratory studies. Many individuals are thus subjected to needless treatment and re-treatment. Prophylactic treatment of contacts is mentioned, and (if this questionable policy is adopted) stress is laid on the importance of enforcing full clinical and serological re-examinations as would be instituted for established infection.

In pregnancy, if it is not possible to differentiate between true and false positive reactions, treatment should be given to protect the foetus, but full surveillance of both mother and child should be insisted on after confinement.

If syphilis is not proved to be the cause of the positive reaction, many patients can be saved the needless stigma and therapy by thorough investigation and by withholding therapy for several months to afford the opportunity of a spontaneous reversal. In these cases, should treatment be considered necessary, the patient must, for practical purposes, be regarded and treated as a latent syphilitic.

"If the original diagnosis of syphilis is accurate, if the original therapy is adequate, and if the physician has a basic understanding of the value and limitations of various serological tests, the frequency and amount of unnecessary re-treatment will be reduced considerably."

D. E.

SPINAL FLUID EXAMINATIONS AMONG PATIENTS WITH PRIMARY OR SECONDARY SYPHILIS. THEODORE J. BAUER, ELEANOR V. PRICE and JOHN C. CUTLER. (1952) *Amer. J. Syph.*, **36**, 309.

Spinal fluid examinations before treatment in primary and secondary syphilis were found to be abnormal in 5% of patients. Reversal of the blood reaction after treatment for secondary syphilis was more satisfactory when the spinal fluid had been negative prior to treatment.

D. E.

SERORESISTANCE FOLLOWING TREATMENT OF SECONDARY SYPHILIS. EVAN W. THOMAS, LOPO DEMELLO and SIMEON LANDY. (1952) *Amer. J. Syph.*, **36**, 319.

Analysis of the records of patients treated for early syphilis with different schedules of penicillin therapy, aqueous and oily solutions, with and without arsenoxide and bismuth. Prolonged seropositivity occurred in approximately 20% of cases in all schedules except in a prolonged course of 600,000 units of penicillin daily for 15 days, and in a further scheme employing one

single injection of 1.2 or 2.4 mega units of penicillin, when seropositivity occurred in 30% of cases. Patients re-treated for relapses or reinfection were more likely to remain seropositive, and treatment with arsenoxide and bismuth in these cases had no appreciable effect on the titre of the serology. The conclusion is drawn that, in all probability, prolonged seropositivity after treatment of early syphilis, in the absence of relapse, reinfection or signs of progression of the disease does not mean a continuance of the syphilitic infection. D. E.

LESIONS OF THE SKULL IN SECONDARY SYPHILIS. ROBERT G. THOMPSON and ROBERT H. PRESTON. (1952) *Amer. J. Syph.*, **36**, 332.

Seven cases showing destructive osteitis of the skull were detected in clinical and x-ray examinations of 80 consecutive patients with secondary syphilis. The lesions were considered characteristic, showing irregular areas of decreased density with a porous worm-eaten appearance. The picture was distinctly different from the proliferation and periosteal thickening seen in gummatous lesions. Treatment was favourable, symptoms rapidly subsiding, but healing was slow. D. E.

THE EPITHELIAL CHANGES IN GRANULOMA INGUINALE. HERMAN BEERMAN and C. E. SONCK. (1952) *Amer. J. Syph.*, **36**, 501.

Histological changes of hyperplasia in granuloma inguinale frequently resemble epithelioma with pearls, mitotic figures, permeations of the basement membrane and anaplastic cells. The reaction in the corium and the presence of Donovan bodies with fibrosis and foci of plasma cells in the healing stage may be of diagnostic value. Malignancy occasionally supervenes on the granulomatous condition. D. E.

CARCINOMA OF VULVA FOLLOWING GRANULOMA INGUINALE. CALVIN R. MACKEY and WILLIAM L. BUNCH, Jr. (1952) *Amer. J. Syph.*, **36**, 511.

A negro woman treated for congenital syphilis at the age of 17 was seen in 1944, when 32 years old, with an ulcerating lesion on the vulva. A diagnosis of granuloma inguinale was made and typical intra-cellular Donovan bodies were detected in the smear, but in spite of several treatments with Fuadin in the subsequent 3 years the lesion did not completely disappear. In 1947 and again in 1951 she was treated with streptomycin and, on biopsy on the latter occasion, the condition was still considered to be only granulomatous in character. Since then the lesion had extended and a recto-vaginal fistula had developed. A further biopsy was made and on this occasion revealed an infiltrating squamous-celled carcinoma. D. E.

THE EFFECT OF A HAND SOAP AND A HEXACHLOROPHENE SOAP ON THE CULTIVABLE TREPONEMATA. ROBERT KELLER and HARRY E. MORTON. (1952) *Amer. J. Syph.*, **36**, 524.

No significant difference between medicated and non-medicated soaps was noted in an evaluation of the high susceptibility of treponemes to soap lather. D. E.

CLINICAL AND SEROLOGIC STUDIES WITH REFERENCE TO SYPHILIS IN GUATEMALA, CENTRAL AMERICA. STUDIES OF COMPARATIVE PERFORMANCE OF THE KAHN, KOLMER, MAZZINI AND VDRL SLIDE TESTS AMONG LEPROSY PATIENTS. JOSEPH PORTNOY, RAMIRO GALVEZ and JOHN C. CUTLER. (1952) *Amer. J. Syph.*, **36**, 566.

In mass serological examinations the incidence of positive reactions was found to be abnormally high and believed to be due to the effect of leprosy. The patients with cutaneous forms of leprosy gave a higher degree of seroreactivity than those in the neural and podalic group. The Mazzini and Kahn tests generally showed greater sero-reactivity than the VDRL and the Kolmer tests. D. E.

THE USE OF HOUSEHOLD DETERGENTS AND THEIR DANGERS. GEOFFREY HODGSON, (1953) *Practitioner*, **170**, 166.

After discussing the chemical nature of household detergents, most of which are anionic, the author points out that the mechanism of cleaning by detergents depends upon a lowering of the surface tension, emulsification and some dissolving of oil and grease, wetting and holding in suspension any soluble particles of dirt, mechanical loosening of dirt particles, and finally rinsing away the solution of the detergent together with suds and lather containing dissolved and emulsified oil and grease and the suspended dirt.

Modern detergents have the advantage over soaps in that they are not inactivated by hardness of water, and they are active in alkaline, acid and neutral solution. Solids are kept suspended in detergent solution and are not re-deposited on to the fabrics during washing. The lower concentration of detergent required—1% as opposed to 5 or 6% with soap, their cheapness and availability when fats are scarce, and their use for skins that are intolerant of soap.

The new powdered detergents require added substances such as trisodium polyphosphate and tetrasodium pyrophosphate to increase the detergent effect and to loosen dirt from the material. Most of the new washing agents contain as much alkaline phosphate as detergent. Carboxymethyl cellulose C.N.C. may also be added to help keep the dirt suspended, as also may colourless fluorescent dyes in a strength of a few parts per million, which give the appearance of a vivid whiteness to the washed materials. Bleaches are not used in detergents.

The way in which detergents act in irritating the skin is not fully understood, but de-fatting and drying probably occur in the same manner as with soaps. Detergents may cause an acute contact dermatitis or a sensitization dermatitis due to degreasing, together with brittleness and breakage of the nails and fissures over the knuckles. Paronychia inflammation may occur most commonly as a result of *Esch. coli* or monilia infection.

The anionic detergents which form the bulk of the household washers are effective only against Gram-positive organisms, and less effective than the cationic against the Gram-negative organisms.

Certain detergents are advertised as not requiring rinsing out but, in view of the fact that cases of dermatitis have occurred from contact with underclothes washed without rinsing, it seems unwise that the omission of rinsing should be advised.

A. C. R.

URTICARIA DUE TO DRUGS OF THE DIGITALIS SERIES. L. S. WOLFE and A. J. GEIGER. (1953) *New Engl. J. Med.*, **248**, 148.

A case of urticaria followed administration of various drugs of the digitalis group. The allergic response was attributed to the cyclopentenophenonthrene nucleus common to these glycosides. Antihistamines did not prevent the reaction.

A. D. P.

MODE OF SPREAD OF CANCER OF THE SKIN. FREDERIC E. MOHS and THEODORE G. LATHEOP. (1952) *Arch. Derm. Syph., Chicago*, **66**, 427.

The first named author has written extensively on the treatment of skin cancers by "chemo-surgery." These cancers are shown by this procedure to have irregular outgrowths which are not clinically evident. These outgrowths follow certain structures, especially the dermis, fascial planes, periosteum, perichondrium, embryological fusion planes, nerve sheaths and lymphatic and blood vessels.

J. K.

FURTHER STUDIES OF THE MOSAIC FUNGUS. E. SILVER DOWDING. (1952) *Arch. Derm. Syph., Chicago*, **66**, 470.

"In cleared preparations of skin taken from mycotic lesions, one often finds patches of refractile debris arranged in a network. This is the much-discussed 'mosaic fungus.'" So the author starts, and goes on, with excellent micro-photographs and diagrams, to show that it is a degeneration product of a dermatophyte. But what of mosaic fungus found in cases which are not dermatophytic infections?

J. K.

THE ADVERSE INFLUENCE OF SYPHILITIC INFECTION ON THE LONGEVITY OF MICE AND MEN. PAUL D. ROSAHN. (1952) *Arch. Derm. Syph., Chicago*, **66**, 547.

Vital statistics show that both treated and untreated syphilitics have a shorter expectation of life than non-syphilitics. A carefully controlled experiment shows that this is also true of mice.

J. K.

SOME OBSERVATIONS ON THE PATHOGENESIS OF PSORIASIS. OSKAR GANS. (1952) *Arch. Derm. Syph., Chicago*, **66**, 598.

The author discusses, briefly, the results of research over the past 40 years into the origin of psoriasis, and refers especially to the altered pH and oxygen consumption of psoriatic lesions. The abstractor has carefully read the article and, especially in view of the demonstration in one part that oxygen respiration is increased in psoriasis and the statement in another that there is a reduction in oxidation, fully agrees with the opening remark that "on taking stock after many years, psoriasis remains a riddle."

J. K.

PRELIMINARY NOTE ON ATHLETE'S FOOT IN BELGIUM. R. VANBREUSEGHEM, P. PETERS and E. TRITSMANS. (1952) *Arch. belg. Derm. Syph.*, 8, 343.

The authors compare the incidence of athlete's foot in 40% of 152 swimmers and 24.5% of 155 gymnasts. But, though they mention, they do not stress the fact that the latter are shod and bathe neither before nor after their exercise.

A. J. K.

SCLEROSING LIPOGRANULOMA. B. T. GALBRAITH and J. M. YOUNG. (1952) *J. Amer. med. Ass.*, 150, 1295.

Two cases of sclerosing lipogranuloma are reported. The first one involved the scrotum, penis and lower abdominal wall, and the process was apparently initiated by repeated tapping of a hydrocoele. The second lipogranuloma developed in the pelvis of a woman who had had multiple laparotomies. One patient obtained some relief from cortisone, but surgical excision is the treatment of choice when practicable.

A. J. R.

THALLIUM INTOXICATION. S. B. FRANK and D. R. HIRSCH. (1952) *J. Amer. med. Ass.*, 150, 586.

Two sisters, aged 2 and 3, developed thallium poisoning after accidental ingestion of rat poison containing thallium salts. In both children alopecia was the presenting symptom. One child showed involvement of the peripheral nerves. Both recovered completely.

A. J. R.

CHRONIC ARSENIC POISONING FOLLOWING USE OF AN ASTHMA REMEDY. A. S. SILVER and P. L. WAINMAN. (1952) *J. Amer. med. Ass.*, 150, 584.

A woman aged 41 receiving an "asthma mixture" containing 0.44 mg. of arsenic trioxide per cubic centimetre developed chronic arsenical poisoning with pigmentation, keratoses, gastroenteritis, hepatitis and mild neuritis. The first pigmentary changes were noted 13 months after starting the mixture.

A. J. R.

ORALLY ADMINISTERED CORTISONE IN ERYTHEMA NODOSUM. S. J. SCHNEIERSON. (1952) *J. Amer. med. Ass.*, 150, 585.

A girl aged 10 with erythema nodosum was treated with oral cortisone. Improvement was noted after 24 hours and the nodules were no longer visible after 48 hours. The lesions did not recur after treatment was discontinued.

A. J. R.

APPRAISAL OF TOPICAL USE OF ANTIHISTAMINES. F. A. ELLIS and W. R. BUNDICK. (1952) *J. Amer. med. Ass.*, 150, 773.

Two hundred dermatologists replied to a questionnaire concerning their experience with topical applications of antihistamines. 94% had tried them, but only 60% still use them, and less than 10% prescribe them regularly. About 25% consider antihistamines to be of some value, especially in anogenital pruritus and localized neurodermatitis. Those who had restricted their use had done so because they considered them ineffective, or because the incidence of sensitization dermatitis was too high. Thephorin was usually considered to be the most frequent cause of dermatitis, but it was also the most popular antihistamine.

A. J. R.

EPIDEMIOLOGICAL AND CLINICAL STUDY OF GRAIN ITCH. B. H. BOOTH and R. W. JONES. (1952) *J. Amer. med. Ass.*, 150, 1575.

Grain itch, the result of infestation with the mite *Pyemotes (Pediculoides) ventricosus*, has been uncommon in the United States during the last forty years. In 1950 and 1951 an epidemic, for which mite-infested straw was responsible, occurred among farmers, strawboard factory workers and others in Indiana. The clinical features of the condition are described and details are given of the life history and distribution of the mite, and methods of treatment and prophylaxis are discussed. The recent abundance of the mite is attributed to a combination of suitable climatic conditions, changed harvesting methods and a decrease of the natural enemies of the host insects.

A. J. R.

TRANSVERSE BAND PIGMENTATION OF FINGERNAILS AFTER X-RAY THERAPY. R. L. SUTTON. (1952) *J. Amer. med. Ass.*, 150, 210.

A negro woman, who had received superficial x-ray therapy to the backs of her hands, developed transverse bands of pigmentation of the finger nails. Melanophores must therefore be present in or under the epithelium of the nail matrix.

A. J. R.

CLINICAL USE OF CORTISONE, HYDROCORTISONE AND CORTICOTROPIN. E. W. BOLAND.
J. Amer. med. Ass., 150, 1281.

All dermatologists who are using the steroid hormones should read this review article, which cannot usefully be abstracted.
A. J. R.

BENIGN AND MALIGNANT DERMAL NEOPLASMS. H. MONTGOMERY. (1952) *J. Amer. med. Ass.*, 150, 1182.

In this interesting general review the common lesions are only very briefly described but the more controversial lesions are discussed in some detail. These include nodular subepidermal fibrosis, blue naevi and Kaposi's disease. The author points out that some of the conditions he includes are not strictly speaking neoplasms.
A. J. R.

BIOLOGICALLY FALSE POSITIVE SEROLOGIC TESTS FOR SYPHILIS. J. E. MOORE and C. F. MOHR. (1952) *J. Amer. med. Ass.*, 150, 467.

This important article should be read by everyone who may be called upon to assess the significance of a positive serologic test. Biologically false positive reactions are of two types, acute and chronic. The acute reactions are particularly associated with various infections and disappear spontaneously within six months of recovery from the infection. The most important of these are: Malaria 100% positive; leprosy 60%; atypical pneumonia 20%; glandular fever 20%; infective hepatitis 10%. Many other infections, bacterial, protozoal and viral, show a biologically false positive in from 2% to 20% of cases.

The chronic biologically false positive reactions persist for long periods, even for a lifetime. The cause is often obscure, but some are a manifestation of serious underlying disease, including the collagen diseases. These chronic false positive reactions are not uncommon, and Moore estimates that in his own practice 43% of persons who would at one time have been diagnosed as latent syphilis are false positive reactors. The introduction of the treponema immobilizing test has been helpful in separating false reactors from latent syphilitics. As its value is well established it is unfortunate that this test is time-consuming and complicated and requires the maintenance of a large rabbit colony as a source of living treponemes.
A. J. R.

HERPETIC URETHRITIS. JUVENAL ESTEVES and MANUEL R. PINTO. (1952) *Brit. J. vener. Dis.*, 28, 205.

A male aged 27 had an herpetic infection of sexual origin. It began as a non-bacterial urethritis which did not respond to chemotherapeutic measures, and in its evolution revealed typical lesions of herpes near the urethral meatus and cutaneous hyperaesthesia, especially in the trunk. The disease developed for 2 months in an undulating form and was cured without relapse. By inoculation on to the chorio-allantoic membrane of chick embryo it was possible to isolate the herpes virus from the urethral secretion.
W. G. A.